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SIMON FLEXNER, M D

PEYTON ROUS, M D

HERBERT S GASSER, M D

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CHEMICAL STUDIES ON BACTERIAL AGGLUTINATION

VII A QUANTITATIVE STUDY OF THE TYPE SPECIFIC AND GROUP SPECIFIC ANTIBODIES IN ANTIMENINGOCOCCAL SERA OF VARIOUS SPECIES AND THEIR RELATION TO MOUSE PROTECTION*

BY ELVIN A. KABAT PH.D C PHILLIP MILLER M.D HILDA KAISER, AND
ALICE Z. FOSTER PH.D

(From the Department of Neurology College of Physicians and Surgeons, Columbia University New York the Neurological Institute of New York, and the Department of Medicine The University of Chicago)

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A specific polysaccharide responsible for the type specificity of Type I meningococci has been prepared by Scherp and Rake (1) and it has been shown that the antipolysaccharide in Type I antimeningococcal horse sera is effective in protecting mice inoculated with virulent Type I meningococci (2) Rake and Scherp stated that in several Type I horse antisera, 90 to 99 per cent of the protective antibodies in the sera could be removed by absorption with Type I polysaccharide (2) In the course of an investigation of the antigenic properties of materials obtained from Type I meningococci, it was noted that several Type I specific antimeningococcal rabbit and chicken sera (3) contained only very small amounts of antipolysaccharide and that after absorption of the antipolysaccharide these sera still contained considerable amounts of type-specific antibody To study this problem, measurements were made by the quantitative agglutinin (4) and precipitin methods (5-7) of the amounts of type-specific and group-specific (species specific) antibodies and of the type-specific antipolysaccharide present in antimeningococcal horse, rabbit, and chicken antisera as well as in sera from a number of individuals convalescing from Type I meningitis By determining the protective power of the sera for mice (8, 9) before and after removal of the different antibodies it was possible to determine with which kinds of antibody protective power was associated

EXPERIMENTAL

Preparation of Bacterial Suspensions—Freshly isolated lyophilized strains of meningococci Type I or II obtained from Dr H. E. Alexander and Dr J. J. Phair were inoculated into peptone blood broth and transferred until good growth was obtained to Difco tryptose phosphate broth or to the casein hydrolysate medium described by Mueller and Hinton (10) prepared without agar 100 ml flasks of broth were inoculated and after 20 hours incubation

* This investigation was carried out under the Commission on Meningococcal Meningitis of the Board for the Control of Influenza and other Epidemic Diseases, Preventive Medicine Service Office of the Surgeon General, U S Army

tion the contents of each 100 ml flask was used for inoculating a flask containing 1 liter of broth. After 24 hours' incubation, the cultures were killed by addition of formalin to a concentration of 1 per cent. The organisms were centrifuged in Sharples centrifuge, and suspended in saline. The bacterial suspension was then heated to 58°C for 45 minutes, and washed seven times with saline. The washed meningococci were suspended in saline containing 0.01 per cent merthiolate and centrifuged lightly to remove debris.

Type I Meningococcus Polysaccharide—A sample of Type I polysaccharide No. 18 (1) was kindly supplied by Dr. H. W. Scherp. This sample was reported by Scherp (11) to contain at least 20 per cent of a second group-specific substance which reacted with antimeningococcal serum. Preparations M6C and M9B₂ were prepared from autolyzed 2 week old cultures of Type I meningococci grown on Difco tryptose phosphate or on casein hydrolysate medium without the use of barium acetate and sodium carbonate or of glacial acetic acid. The broth was concentrated by ultrafiltration and the polysaccharide obtained by repeated precipitation with 4 volumes of alcohol, and removal of protein by saturation with ammonium sulfate. The solution was then dialyzed and the polysaccharide precipitated with safranin, the safranin was removed by repeated solution in 20 per cent sodium acetate and precipitation of the polysaccharide with alcohol. In the case of M9B₂, fractional precipitation with methyl and ethyl alcohol was used instead of safranin. These preparations appeared to contain only traces of group specific substances. Their properties have been described in detail (16).

Antisera—Type I horse antimeningococcal serum H1095 was obtained from Dr. Jules Freund of the New York City Department of Health Laboratories. The pool (Rx) of Type I antimeningococcal rabbit sera was provided by Dr. H. E. Alexander and the other Type I rabbit serum (RL) was obtained from Lederle Laboratories. Types I and II antimeningococcal chicken sera were prepared by immunizing chickens with live cultures of Types I and II meningococci as described by Phair, Smith, and Root (3). Sera from convalescent meningitis cases were obtained from Presbyterian, Babies, Willard Parker, and Mount Sinai Hospitals and from the U. S. Marine Hospital, Staten Island, through the courtesy of Drs. R. F. Loeb, H. E. Alexander, R. Ottenberg, G. Schwartzman, and L. Sofian. All patients had received sulfonamide treatment and the sera were obtained after about 1 week of convalescence or shortly before discharge from the hospital.

Quantitative Determination of Antibody N—The total agglutinin N and the group-specific agglutinin N present in the antisera were measured by the quantitative agglutinin method described in (4) using suspensions of Type I and Type II meningococci respectively. The Type I antipolysaccharide in the horse and rabbit sera was determined at 0°C by the quantitative precipitin method (5) and the antipolysaccharide content of the chicken and human sera was estimated by the micro method devised by Heidelberger and MacPherson (6) and described in greater detail in (7). The modified Folin Ciocalteu tyrosine reagent was used and calibration curves were obtained with electrophoretically separated chicken and human gamma globulin solutions respectively. Before measuring the agglutinin or precipitin content of the human or chicken sera, the complement was first removed on the precipitate formed by addition of 0.045 mg egg albumin N and 0.40 mg antiegg albumin N per 4.5 ml serum as recommended by Heidelberger and Mayer (12). A summary of quantitative immunochemical methods is given in (13).

Mouse Protection Tests—With the stronger sera, the standard U. S. Public Health Service procedure described by Branham (14) was used in which varying doses of serum are given followed by an injection of 100,000 M.L.D. of meningococci in mucin suspension. The protection tests were carried out with a different strain of Type I meningococci than was used for the quantitative agglutinin determinations. With weaker sera or when only small quantities of serum were available, a constant dose of serum was injected per mouse followed by varying doses of meningococci. The protective power of each serum after absorption with Type I

and Type II suspensions and with various polysaccharide preparations was compared with a similarly diluted control of unabsorbed serum and saline. The results in Tables II and III are expressed as the percentage of the original protection potency remaining in the supernatant.

RESULTS

Table I summarizes the data on the potency of the various sera in protecting mice against Type I meningococci. It may be noted that the most potent sera were the horse and rabbit therapeutic Type I sera (H1095 and RL) and that the chicken and human sera were much less effective. A comparison of the protective power of the sera with the total agglutinin N content, determined

TABLE I

Protective Potency of Horse (H) Rabbit (R) Chicken (C) Type I Antimeningococcus Sera and of Sera from Human Convalescents (M)

Serum No	Type	Antibody N removed per ml serum by Type I meningococci mg	Serum dilution protecting against Type I meningococci		
			100,000 M.L.D.	10,000 M.L.D.	1000 M.L.D.
H1095	I	1.15	1/400 - 1/800	1/350	1/30
II antitoxin	?	0.56			
Rx (pool)	I	0.24			
RL	I	0.50	1/4000-1/8000	1/10-1/20	1/10-1/20
C85 ₁	I	0.55	1/15		
M8 2		0.12			
M10 1	I	0.06	1/60-1/70		
M10 2	I	0.10	1/15-1/30		
M14 2		0.05	1/20		
M18 2	?		1/20		

Additional sera tested: M9 failed to protect against 10 M.L.D. in 1/20 dilution. M18 1 failed to protect against 1000 M.L.D. in 1/4 dilution.

* 0.5 ml serum dilution used per mouse.

with a Type I meningococcus suspension, indicates no correlation of antibody nitrogen content and protective power even among sera of the same animal species.

In Table II, measurements of the Type I and Type II agglutinin N and the Type I antipolysaccharide content of the horse, rabbit, and chicken sera are given, together with values for the fraction of mouse protective activity remaining in the supernatant after removal of these different antibody fractions. It may be noted that with sera H1095, RL and C84₁, 84₂, and 85₁, the total Type I agglutinin N content was considerably greater than the sum of the Type II agglutinin N and the antipolysaccharide N removed with purified preparations M6C or M9B₁, indicating the presence of other Type I specific antibody in these sera besides the antipolysaccharide. In all these sera except

H1095, the antipolysaccharide content as measured with poly-saccharide preparation 18 (Scherp) was only very slightly higher than that obtained with the other samples.

In all of the rabbit and chicken Type I sera, removal of the antipolysaccharide with any of the three samples of polysaccharide or of the Type II agglutinin left most of the protective antibody in the supernatant, but absorption with the homologous Type I suspension effected complete or almost complete

TABLE II

Antibody Activity and Mouse Protection Determined from *Artemeningococcus* Horse (H), Rabbit (R), and Chicken (C) Serum. Types I and II Meningococci and by Purified Type I Meningococcus Polysaccharide

Serum	Antiserum to men- gococcus type	Antibody N removed per ml of serum by				Percentage of protective power against Type I meningococci in supernatant after absorption with			
		Meningococcus cells		Type I poly- saccharide		Meningococcus cells		Type I poly- saccharide	
		Type I	Type II	Prepara- tion 18 (Scherp)	M6C or M9B	Type I	Type II	Prepara- tion 18 (Scherp)	M6C or M9B
		mg/ml	mg/ml	mg/ml	mg/ml	per cent	per cent	per cent	per cent
H1095	I	1.15	0.70	0.71	0.54	0	100	60-70	40-50
H antitoxin	"	0.56	0.58						
Ix (pool)	I	0.24	0.11	0.04	0.015	0	100	90-100	90-100
KI	I	0.50	0.01	0.11	0.09	10	100	50†	50-100
C84 ₁	I	0.10	0.25		0.03*				
C84	I	0.25	0.16	0.002*	0.002*				
C85 ₁	I	0.55	0.28	0.061*	0.019*	0	90	90-100	90-100
C135	II	0.20	0.32		0.005*				

* Determined by micro method using John Ciocalteu reagent (6, 7)

† A 1/1600 dilution of this supernatant protected against 100 000 lethal doses, as compared with a 1/3200 dilution of a control of serum with saline

removal of the protective antibody (Table II). With a Type II chicken antiserum, C135, conversely, the Type II suspension removed more antibody N per milliliter of serum than did the Type I suspension. The very small amount of Type I antipolysaccharide found may have been due to traces of group-specific antigen in the polysaccharide preparation. It is also of interest to note that after a second course of immunization, C85 showed a decrease in total antibody N with almost complete disappearance of the antipolysaccharide although the Type I agglutinin still remained considerably higher than the Type II agglutinin.

In the case of H1095, more than twice as much antibody N was taken out with preparation 18 than with M6C or M9B. This additional amount of antibody N was not protective antibody since preparation 18 did not remove

any more of the protective antibody than did the other two polysaccharides (Table II). Some of this additional antibody removed by Scherp polysaccharide, although not protective, was shown to be Type I specific by absorption experiments in which after removal of the antipolysaccharide from two samples of serum with M6C and with preparation 18, both supernatants still contained the same amount of Type II agglutinin. Subsequent addition of Type I meningococcus suspension then showed the preparation 18 supernatant to con-

TABLE III

Antibody Nitrogen and Mouse Protective Power Removed from Sera of Patients Convalescing from Meningococcus Meningitis by Types I and II Meningococci and by Purified Type I Meningococcus Polysaccharide

Case No.	Type	Antibody N removed per ml. of serum by				Percentage of protective power against Type I meningococci in supernatant after absorption with			
		Meningococcus cells		Type I polysaccharide		Meningococcus cells		Type I polysaccharide	
		Type I	Type II	Preparation 18 (Scherp)	M6C or M9B ₁	Type I	Type II	Preparation 18 (Scherp)	M6C or M9B ₁
		mg./ml	mg./ml	mg./ml	mg./ml	per cent	per cent	per cent	per cent
4	I	0.03	0.03	0.000	0.000				
8 2	?	0.12	0.07	0.027	0.004	0	100	100	>50
9 1	I	0.04	0.04	0.000	0.000				
9 2	II	0.01	0.01	0.000	0.000				
(Acute phase)									
9 2	II	0.00	0.01	0.000	0.000				
10 1	I	0.06	0.08	0.008	0.010	10-20	100	12-25	50
10 2	I	0.10	0.10	0.007	0.005	0	100	50	100
11 1	?	0.00	0.01	0.000	0.000				
11 2	I	0.01	0.05	0.010	0.015				
14 1	?	0.00	0.00	0.001	0.001				
14 2		0.05	0.00	0.003	0.003	0	100	100	100
A Normal		0.00	0.00						
B Normal		0.00	0.00						

tain less antibody N than did the M6C supernatant. In this absorption experiment, the supernatants after removal of the antipolysaccharide with any of the three preparations and of the Type II agglutinin with Type II suspension, still contained considerable amounts of protective antibody which was completely removed with a Type I meningococcus suspension. The horse anti-meningococcus antitoxin was found to contain only group-specific antibody since both Type I and II suspensions removed equal amounts of antibody nitrogen.

The antibody response of a number of humans recovering from meningococcus meningitis is given in Table III. In practically all of these the amount of agglutinin N found with Type II suspension was, within the limit of error,

the same as with Type I suspension indicating that the bulk of the antibody formed was group specific. Most of this antibody was probably not protective antibody, since with sera 10 I and 10 2, removal of the antibody N with Type II suspension left all of the protective power in the supernatant. Amounts of protective antibody too small to affect the value for Type I agglutinin N were present, however, since absorption with Type I organisms removed most or all of the protective antibody from these sera without affecting the total agglutinin N. Some of this protective antibody was antipolysaccharide which constituted but a small proportion of the total antibody N.

Two sera (cases 8 2 and 11 2) showed a different type of antibody response, resembling more closely the rabbit and chicken sera in Table II. In these sera more Type I agglutinin was present than Type II agglutinin. This difference could not be accounted for by the antipolysaccharide present and protective activity could only be removed from the serum by absorption with homologous Type I meningococcus suspension. In the case of serum 8 2, more antibody N was taken out of the serum with preparation 18 than with M6C or M9B, but this antibody did not appear to be associated with mouse protection (*cf.* H1095 Table II). With serum 11 2, the removal of the antipolysaccharide also failed to lower the protective antibody in the supernatant.

Several normal human sera were found to contain no measurable agglutinin to Type I and Type II organisms, nor was any antipolysaccharide found in over 50 normal human sera.

DISCUSSION

The problem of outlining the antigenic composition of meningococci and determining the chemical nature of the substances which produce protective antibody on immunization has been complicated by the fact that the principal antigens which stimulate antibody formation are group-specific and that these antibodies have little or no protective power. Although both pneumococci and Type I meningococci possess type specific polysaccharides which induce the formation of protective antibody, in both horse and rabbit antisera to the former group the antipolysaccharide comprises by far the largest portion of the total antibody (4, 12), whereas in the latter group it generally consists of only a small fraction of the total antibody (11). This explains the failure to demonstrate any correlation between the total Type I agglutinin N in the sera and their protective potency' (Table I).

By correlating the total Type I and Type II agglutinin N, the antipolysaccharide content, and the relation of these antibodies to mouse protection it has been possible to demonstrate that rabbit and chicken Type I antimeningococcal sera contain type-specific antibodies capable of protecting mice against inoculation with virulent Type I meningococci. A portion, at least, of these antibodies are distinct from the antibody to the Type I polysaccharide as determined with three different polysaccharide preparations (Table II).

In a Type I horse antiserum, also, more protective antibody was found than could be removed by the Type I polysaccharide, although in this serum the antipolysaccharide was found to be responsible for a considerably larger portion of the total protection. This does not necessarily conflict with the findings of Rake and Scherp (2) that in several Type I antisera all of the protective activity was due to antipolysaccharide, since the antibody response of different horses may be expected to vary over a wide range and also since the Type I polysaccharide appears to be a much better antigen in the horse than in the rabbit, chicken, or in man (Tables II and III).

In human meningococcal meningitis cases treated with sulfonamides, the antibody formed is, in most instances, group-specific antibody as measured by the quantitative agglutinin methods. Although some protective antibody is formed in these cases as well, the data indicate that the total weight of protective antibody, including the Type I antipolysaccharide, is not large enough to be measurable by the quantitative agglutinin method. This may in part account for the failure of Thomas, Smith, and Dingle (15) to find any correlation between the degree of antibody response as measured by the usual agglutination tests and the severity or duration of illness. In two cases (82, 142), however, more Type I agglutinin N was found than could be accounted for by the sum of the Type II agglutinin and the Type I antipolysaccharide, and protective activity was associated with this residual Type I agglutinin, as was found to obtain with the animal antisera. The amounts of total agglutinin N and of antipolysaccharide N found in the serum of patients recovering from meningitis are of the same order as those found by Heidelberger and Anderson for anti "C" and type-specific antipolysaccharide accompanying convalescence from pneumonia (7), indicating a similar wide individual variation in the human immune response to rapidly terminating infections.

As yet, nothing is known about the chemical nature of the antigen responsible for the production of this new Type I specific protective antibody. Although the evidence indicates that the Type I polysaccharide, even when prepared by methods which avoid the use of strong acid or alkali, does not react with antibody to this antigen, it is quite possible that the latter consists of polysaccharide bound to some other as yet unidentified constituent in the intact meningococcus and that either autolysis of the organism or the method of preparation liberates the polysaccharide. However, it is equally possible that this other antigen is entirely unrelated to the Type I polysaccharide.

In any event, the present study provides a very direct approach to the purification and isolation of this substance from the meningococcus, since by absorption both of the Type I antipolysaccharide and of the group-specific agglutinin from the animal sera, antisera specific for this antigen could be obtained and used as a guide to chemical isolation. Since this antigen is both Type I specific and associated with the production of protective antibodies the possibility that, if obtainable in pure form, it might provide an effective

antigen for active immunization of humans against Type I meningococcal meningitis should not be overlooked

SUMMARY

1 The quantitative method for the estimation of agglutinins has been applied to antimeningococcal horse, rabbit, and chicken sera and to the sera of humans convalescing from meningococcus meningitis. The type-specific and group specific agglutinin N can be measured, using homologous and heterologous suspensions of meningococci.

2 Type I horse, rabbit, and chicken antimeningococcal sera contain considerable amounts of antibody which cannot be removed either by Type II meningococcus suspension or by preparations of the Type I specific polysaccharide. This residual type specific antibody has marked potency in protecting mice against subsequent infection with meningococci.

3 Most human convalescent sera contain group specific antibody. Small amounts of protective antibody and of antipolysaccharide are also formed.

4 Type I antiserum absorbed with Type I polysaccharide and with Type II meningococci could be used as a guide in the purification of this new antigen.

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OBSERVATIONS ON THE SITES OF REMOVAL OF BACTERIA FROM THE BLOOD IN PATIENTS WITH BACTERIAL ENDOCARDITIS

By PAUL B. BEESON, M.D., EMMETT S. BRANNON, M.D.,
AND JAMES V. WARREN, M.D.

(From the Medical Service of Grady Hospital and the Department of Medicine, Emory University School of Medicine, Atlanta)

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The number of bacteria in the peripheral blood of a patient with bacterial endocarditis is nearly always relatively small, despite the fact that organisms appear to have free access to the circulating blood. This indicates that some mechanism is constantly at work to remove them from the blood. Opinions on the means of this removal have differed, some have considered a bactericidal action of the blood itself to be responsible, while others have held that the circulating bacteria are arrested in particular parts of the body.

If bacteria are removed from the blood in certain organs, one would expect to find fewer organisms in venous blood which has just passed through those organs than in the blood entering them, while if a bactericidal action of the blood is responsible there should be no marked difference in the bacterial content of the blood in different parts of the body. The present communication deals with quantitative arterial and venous blood cultures in six patients with bacterial endocarditis. Blood was obtained not only from peripheral arteries and veins but also from such locations as the right auricle, the venae cavae, the hepatic, and renal veins. A comparison of the colony counts obtained in serial samples from these areas has provided information in regard to the mechanism of removal of bacteria from the blood.

Methods

In all tests the plan was to obtain paired samples of blood at intervals from two different locations in the blood stream—usually the pairs consisted of one arterial and one venous sample although occasionally two venous ones were taken. All arterial blood was drawn from femoral arteries, on the assumption that the bacterial content of blood in all arteries (excepting the pulmonary) would be approximately the same at any one time. It is realized that this may not always be the case since infected particles which break off from the vegetations would not be distributed equally in the arterial tree.

Each pair of samples was collected by two persons, and every effort was made to maintain a uniform time relationship between them, i.e. to collect the arterial blood about 5 seconds before the venous blood. When two venous samples were being paired they were drawn simultaneously. Technical difficulties were encountered occasionally so that this time relationship was not obtained in every instance. A separate dry sterile syringe was used for each sample.

In obtaining blood from vessels in the extremities an inlying needle of the Ungar type was used. This needle has a snug fitting stylet which can be withdrawn to permit a syringe to be

attached, then after blood has been taken the stylet can be replaced. Thus allows repeated sampling from one vessel without multiple puncture.

To obtain blood from the right auricle, vena cava, renal and hepatic veins, the technique of right auricular catheterization developed by Courmand and his associates (1) was used. In this procedure a special flexible radiopaque ureteral type catheter is inserted into an antecubital vein and is pushed, under fluoroscopic guidance, through the veins of the arm and axilla into the superior vena cava and from there on into the right auricle. In order to prevent clotting of blood in the catheter a slow drip of physiologic saline is run through it from a reservoir attached to the side arm of a three way stopcock. When blood is to be taken the flow of saline is switched off and suction is applied to the catheter by means of a sterile syringe. The capacity of the catheter is approximately 1.0 cc., and in order to avoid dilution of the test specimen by saline in the catheter, the first 3.0 cc. which are withdrawn are discarded. A fresh sterile syringe is then attached and the specimen of blood to be examined is drawn into it. Following this the flow of saline through the catheter is resumed.

By an extension of the foregoing method specimens of blood were also obtained from the hepatic and renal veins. Technical details have been given elsewhere (2, 3).

The volume taken for each culture was 1.5 to 2.0 cc. of blood. This was transferred to a sterile test tube containing 25 mg. dry sodium citrate, and the mixture was agitated sufficiently for thorough mixing of the anticoagulant. The tube was then labeled and placed in a rack in ice water, where it remained until the conclusion of the sampling.

One agar pour plate was made from each sample. One cc. of blood was measured in a serologic pipet and transferred to a Petri dish. The blood was then mixed with 20 cc. of warm agar base (Disco). The mixture was allowed to solidify at room temperature, and then incubated at 37° C. for 48 to 72 hours.

Each colony count was made with the aid of a modified "Quebec" colony counter, by two persons. In most instances the two results were very close, and the mean was the figure accepted. In a few instances where the difference was greater than 10 per cent. the counts were repeated until better agreement was obtained.

PATIENT 1

Patient 1—No. 142778. A 33 year old negro male, admitted to Grady Hospital on July 22, 1943. There was no history of rheumatic fever or syphilis. His illness had begun 6 months previously, with weakness, fever, headache, nausea, and pains in fingers and toes. While in the hospital his temperature ranged between 101 and 103° F. Physical examination disclosed typical signs of aortic insufficiency, petechial hemorrhages in skin and conjunctivae, and palpable spleen. Urine usually contained red blood cells. The Kahn test was positive on two occasions. Eleven blood cultures all yielded *Streptococcus viridans*. Sulfadiazine therapy had no obvious effect on the disease. The studies on his bacteremia reported here were done on Aug. 4, 1943. He died on Aug. 9, 1943, following a cerebral embolism. Permission for autopsy was not granted.

The results of a series of 31 blood cultures on this patient during a period of 69 minutes are shown in Table I. Sixteen of the samples tested were from the femoral artery, these were paired with blood from the femoral vein, the hepatic vein, the superior vena cava, and the right auricle. The colony counts on the arterial blood during the entire period ranged from a low of 357 to a high of 642. The first comparison was with femoral vein blood, where the colony counts in 4 samples were found to be somewhat lower than in arterial blood, ranging

between 235 and 319. Next, 4 samples of blood from one of the hepatic veins were tested, and here a striking difference resulted. Colony counts in the liver blood were, respectively 6, 10, 9, and 6. These figures are all less than 3 per cent of the level prevailing in arterial blood throughout the experiment. Four samples of blood from the superior vena cava gave counts varying between 283

TABLE I

Patient 1 Colonies per Cubic Centimeter in Blood from Femoral Artery Femoral Vein, Hepatic Vein Superior Vena Cava, and Right Auricle

Time	Femoral artery	Femoral vein	Hepatic vein	Superior vena cava	Right auricle
<i>a.m.</i>					
10 43	357				
10 45	375				
10 48	448				
10 50	476				
10 52	545	244			
10 54	377	Cl			
11 02	482	235			
11 03	446	295			
11 05	486	319			
11 25	Cl.		6		
11 27	440		10		
11 30	374		9		
11 32	466		6		
11 38	401			283	
11 40	Cl			294	
11 41	449			310	
11 43	Cl			346	
11 50	642				279
11 51	Cl				287
11 52	387				239

Cl.—specimen lost because of clotting.

and 346, while in 3 samples of mixed venous blood from the right auricle the counts were found to be 239, 279, and 287.

Patient 2—No 146223. A 17 year old negro girl, admitted to Grady Hospital on July 20 1943. Her illness had begun 4 months previously, with fever and polyarthritides. Examination disclosed typical signs of mitral stenosis, petechiae in conjunctivae and skin and palpable spleen. Her temperature varied between 100 and 102 F. Seven blood cultures were negative. On sulfadiazine therapy she improved somewhat and returned to her home. She continued to have fever however and gradually developed signs of cardiac decompensation. On Nov 6 1943 she had a cerebral accident and became comatose. Was readmitted Nov 8

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1943 Blood cultures were then positive for *Streptococcus viridans*. The studies on her bacteremia reported here were done on Nov. 10, 1943 and Nov. 11, 1943. She died on Nov. 14, 1943. Autopsy revealed rheumatic mitral stenosis, with vegetations on the mitral leaflets and also on the adjacent wall of the left ventricle.

The first studies on this patient's bacteremia are shown in Table II. Cultures were made from blood in a femoral artery, a femoral vein, an hepatic vein, and the right auricle. Thirty-four samples of blood were collected from these

TABLE II

Patient 2. Colonies per Cubic Centimeter in Blood from Femoral Artery, Femoral Vein, Hepatic Vein, and Right Auricle

Time	Femoral artery	Femoral vein	Hepatic vein	Right auricle
a.m.				
9 22	143	68		
9 29	161	63		
9 35	116	46		
9 46	118	56		
9 52	106	85		
9 58	112	67		
10 10	123	94		
10 18	Cl	88		
10 32	125	140		
10 43	128	115		
11 18	193		9	
11 21	201		3	
11 24	196		7	
11 28	182		6	
11 30	Cl		7	
11 32	122		2	
11 41	192			119
11 44	154			109

Cl—specimen lost because of clotting

locations during a period of 142 minutes. Colony counts in 16 specimens of arterial blood ranged from 106 to 201. In 10 samples of femoral vein blood the range was from 46 to 140, and in all but one instance (10 32 a.m.) the count on the venous blood was below that of the corresponding arterial sample. In the next portion of this period 6 samples of hepatic vein blood were cultured, and here the colony counts varied between 2 and 9. In each instance this was less than 5 per cent of the count on the arterial sample with which it was paired. At the conclusion of the period 2 samples of mixed venous blood from the right auricle were cultured. These gave considerably lower colony counts than the

corresponding samples of arterial blood—119 and 109, contrasted with 192 and 154.

On the following day samples from the femoral artery and the antecubital vein were cultured. The results are shown in Table III. Unfortunately one of the venous blood cultures was contaminated and could not be counted. Very little difference was found between blood samples from these sources: in 3 of the 4 pairs the results were almost identical, while in the fourth the venous colony count was approximately 80 per cent of the arterial.

Patient 3—No 163684. A 40-year-old negro male admitted to Grady Hospital on Jan. 21, 1944. Ten days previously he had developed a respiratory infection, and 5 days later he had become acutely ill, with severe headache, stiff neck, and fever. On admission he had signs of meningitis, which were found to be due to pneumococcus Type 24. He was given sulfadiazine by mouth and penicillin intrathecally. Signs of meningitis improved, but he continued to

TABLE III

Patient 2: Colonies per Cubic Centimeter in Blood from Femoral Artery and Antecubital Vein

Time	Femoral artery	Antecubital vein
<i>a.m.</i>		
8:58	203	194
9:00	228	181
9:02	226	Contam.
9:10	164	163
9:14	175	176

Contam.—contamination of culture.

have fever and blood cultures were repeatedly positive for pneumococcus Type 24. Antibodies for this organism were present in his blood serum. He had physical signs of aortic insufficiency. The studies on his bacteremia reported here were done on Jan. 25, 1944, Feb. 2, 1944, and Feb. 5, 1944. He died on Feb. 11, 1944. Autopsy revealed vegetations of bacterial endocarditis located on the mitral and aortic valves.

Three separate studies were done on this patient's bacteremia. The first is shown in Table IV. Thirty-six samples of blood were taken from the femoral artery, the inferior vena cava, the hepatic vein, and the right auricle during a period of 54 minutes. There appeared to be more fluctuation in the colony count in the arterial blood of this patient than in the other subjects, since during the period of observation the range in colony count was from a low of 53 to a high of 697. The first 6 samples of venous blood were taken from the inferior vena cava, at a point between the level of the renal veins and the heart. In the first 2 the venous colony count was higher than the arterial, while in the last 4 it was about equal or lower. Obviously no conclusion can be drawn from this result. The next samples of venous blood were taken from one of the hepatic veins. During the period of time these were being taken there was a marked

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variation in the arterial colony count. A similar pattern of change also held for the hepatic vein colony count, although it was considerably lower in each instance, being from 10 to 25 per cent of the corresponding arterial count. In the final part of this study 6 samples of mixed venous blood were taken from the right auricle. The first of these gave a higher count than its arterial mate, the next was slightly lower, and in the remaining 4 the level was considerably lower, although not so low proportionately as in the case of hepatic vein blood.

TABLE IV

Patient 3. Colonies per Cubic Centimeter in Blood from Femoral Artery, Inferior Vena Cava, Hepatic Vein, and Right Auricle

Time	Femoral artery	Inferior vena cava	Hepatic vein	Right auricle
<i>p.m.</i>				
2 34	144	246		
2 36	104	226		
2 38	305	203		
2 40	247	244		
2 42	201	187		
2 44	246	172		
2 52	63		7	
2 57	197		50	
2 59	673		103	
3 02	697		121	
3 04	377		55	
3 06	109		11	
3 15	86			161
3 17	98			91
3 22	100			58
3 24	76			36
3 26	92			63
3 28	53			34

Table V contains the results of another series of blood cultures in the same patient. First femoral arterial blood was compared with blood from the right renal vein. In 10 pairs of cultures the arterial colony count was higher than the venous count 9 times, although in some of these the difference was slight, and in no instance was the venous count less than 60 per cent of the arterial. In the second part of this study a comparison of femoral vein and antecubital vein blood was made. Nine pairs of samples were obtained, and in 8 of these the antecubital vein count was considerably higher than the femoral vein count. In only one pair (2 38 p.m.) was the count higher in femoral vein blood and here the figures were almost the same 110 and 112.

TABLE V

Patient 3 Colonies per Cubic Centimeter in Blood from Femoral Artery Renal Vein Antecubital Vein and Femoral Vein

Time	Femoral artery	Renal vein	Antecubital vein	Femoral vein
<i>p.m.</i>				
1 50	303	249		
1 52	356	248		
1 55	216	316		
1 57	366	357		
1 58	203	144		
2 00	288	214		
2 02	312	294		
2 04	304	201		
2 06	248	179		
2 07	301	270		
2 25			152	114
2 29			121	81
2 31			156	92
2 33			107	80
2 38			110	112
2 39			101	71
2 41			149	65
2 43			84	41
2 45			83	58

TABLE VI

Patient 3 Colonies per Cubic Centimeter in Blood from Femoral Artery and Antecubital Vein

Time	Femoral artery	Antecubital vein
<i>p.m.</i>		
1 00	266	228
1 03	264	251
1 05	300	285
1 07	358	256
1 08	399	397
1 11	340	358
1 13	397	344
1 15	298	318
1 17	332	342
1 20	552	533
1 23	671	534

The third series of observations on patient 3 is presented in Table VI. This consisted of a comparison of arterial and antecubital vein blood. Eleven pairs of samples were taken. In 8 of these the arterial count was higher than the

venous, while in 3 the venous count was higher. It should be noted that in 4 of the instances in which the arterial count was higher the difference was comparatively small, and that in no pair was the venous count less than 70 per cent of the corresponding arterial sample.

Patient 4—No. 200706. A 20 year old negro woman, admitted to Grady Hospital on Feb. 10, 1944. She gave a history of rheumatic fever at the age of 6 and a diagnosis of aortic insufficiency had been made when she was 18. She stated that she had felt well until Feb. 9, 1944, the day before admission to the hospital, when she noted fever, headache, and joint pains. During the next 3 days her temperature ranged between 101 and 103° F. and 4 blood cultures yielded *Streptococcus viridans*. The studies of her bacteremia reported here were done on Feb. 13, 1944. She was treated with sulfadiazine for the next 8 days. This caused a drop in temperature, but blood cultures remained positive. She was then given penicillin, 250,000 units daily, for 14 days. Blood cultures became negative and have remained so since. When last examined, on Sept. 2, 1944, she was afebrile and showed no other sign of return of the infection.

During one period of 52 minutes, 46 samples were secured for culture. Arterial blood was paired successively with that from a renal vein, an hepatic vein, and the right auricle. The results are given in Table VII. In the first 7 pairs colony counts on arterial blood ranged from 89 to 132, while those on renal vein blood ranged from 92 to 114. In one instance the venous count exceeded the arterial, in another the counts were exactly the same, and in the remaining 5 pairs the venous counts were 79 to 89 per cent of the arterial counts. These figures do not warrant definite conclusions, but they suggest that in general the colony count in blood which has passed through the kidneys is slightly lower than the colony count in arterial blood.

In the next series of 8 pairs, samples of blood were collected from an hepatic vein as well as from the femoral artery. During this time the arterial colony counts varied between 80 and 110, whereas in liver blood the range was from 25 to 57. In actual percentages the hepatic vein counts were 25 to 71 per cent of the arterial. In this patient the proportionate number of colonies in hepatic vein blood was higher than was found in any of the other patients in this series, nevertheless, even here there appeared to be a very considerable reduction in the bacterial content of hepatic vein blood.

Finally 8 observations were made on the difference between arterial blood and mixed venous blood from the right auricle. During this period arterial colony counts varied between 92 and 121, while the figures for auricle blood were from 64 to 97. Considering individual pairs, the right auricle counts were 67 to 83 per cent of the corresponding arterial levels. Here then, as in all other cases in this series the bacterial content of mixed venous blood returning to the heart was consistently found to be lower than that of the arterial blood.

Patient 5—No. 158290. A 27 year old negro woman, admitted to Grady Hospital on Jan. 23, 1944. Her illness had begun 11 weeks previously, with fever and polyarthritis. On the

day before admission she suffered a subarachnoid hemorrhage. Examination revealed stiffness of the neck, petechial hemorrhages in conjunctivae, signs of mitral stenosis and aortic insufficiency palpable spleen. Spinal fluid was blood tinged. Blood culture yielded *Streptococcus viridans*. The studies on her bacteremia reported here were done on Jan. 28 1944. She died on Feb. 11 1944. Autopsy revealed rheumatic heart disease and extensive vegetations of bacterial endocarditis on both valves of the left heart.

TABLE VII

Patient 4 Colonies per Cubic Centimeter in Blood from Femoral Artery Renal Vein Hepatic Vein and Right Auricle

Time	Femoral artery	Renal vein	Hepatic vein	Right auricle
<i>p.m.</i>				
3 37	89	114		
3 42	113	101		
3 44	102	102		
3 46	116	92		
3 48	132	114		
3 49	115	98		
3 52	113	94		
3 56	80		57	
3 58	95		50	
3 59	81		32	
4 01	102		38	
4 03 ³⁰	101		25	
4 04	106		46	
4 06	92		40	
4 08	110		36	
4 18	109			91
4 19	108			87
4 21	95			64
4 22	104			85
4 24	105			97
4 25	121			92
4 26	92			72
4 29	107			86

In Table VIII are the findings in 46 blood cultures taken during a period of 91 minutes. Arterial blood was paired with venous blood from the inferior vena cava, the right auricle, and an hepatic vein, then several samples were collected from a femoral vein and an antecubital vein. The general level of the bacteremia in this patient was the lowest in this series, furthermore there appeared to be a greater proportionate variability in the colony counts from minute to minute than had been observed in the other subjects.

The colony count in samples from the inferior vena cava (below the level of

the renal vein) exceeded that of arterial blood in one instance, it was the same in another, while in the remaining 4 pairs the arterial count was higher than the venous. The colony counts in 4 of 5 samples of mixed venous blood from the right auricle were considerably lower than those of the corresponding arterial samples, in the fifth pair the venous count was 5 when the arterial count was 4.

TABLE VIII

Patient 5. Colonies per Cubic Centimeter in Blood from Femoral Artery, Inferior Vena Cava, Right Auricle, Hepatic Vein, Femoral Vein, and Antecubital Vein.

Time	Femoral artery	Inferior vena cava	Mixed arterial	Hepatic vein	Femoral vein	Antecubital vein
1 31	9	6				
1 33	12	12				
1 35	9	8				
1 36	5	3				
1 35	11	13				
1 40	17	9				
1 51	15		5			
1 52	9		1			
1 54	1		5			
1 55	12		1			
1 57	19		6			
2 21	8			0		
2 22	6			2		
2 24	11			1		
2 26	15			1		
2 28	9			2		
2 48					20	21
2 50					10	18
2 52					15	11
2 54					10	14
2 59					12	16
3 01					7	18
3 02					19	21

A definite reduction in colony count in hepatic vein blood was observed in this patient. In 5 samples the colony counts were 0, 1, 1, 2, and 2, during the same period the femoral artery colony counts varied between 6 and 15.

Lastly, femoral vein samples were compared with blood from an antecubital vein. Seven specimens were obtained from each source. In one instance the count was higher in femoral vein blood, but in the remaining 6 pairs it was higher in antecubital vein blood. This is in line with the previous observations,

that the bacterial content of blood in an antecubital vein is nearer to the arterial level, than that of blood from a femoral vein

Patient 6—No. A99095 A 20 year old white woman admitted to Grady Hospital on Apr 17 1944. She gave no history of rheumatic fever. Her illness had begun 6 months previously with fever and malaise later there was a polyarthrititis which varied in intensity. On two

TABLE IX

Patient 6 Colonies per Cubic Centimeter in Blood from Femoral Artery Renal Vein, Hepatic Vein and Right Auricle

Time	Femoral artery	Renal vein	Hepatic vein	Right auricle
<i>p.m.</i>				
1 45	195	194		
1 47	245	195		
1 49	199	180		
1 51	226	174		
1 53	223	196		
1 55	236	210		
1 57	209	188		
1 59	286	210		
2 03	188		5	
2 05	220		6	
2 06	266		12	
2 08	276		8	
2 10	249		6	
2 12	227		5	
2 14	277		4	
2 16	288		7	
2 20	284			186
2 22	253			207
2 24	283			151
2 26	319			156
2 28	259			173
2 30	250			203
2 32	322			230
2 34	297			209

occasions she had suffered paralysis of the extremities both of which had cleared almost entirely. She had noted painful spots in the tips of her fingers. Her temperature varied from 101 to 104 F. Physical examination revealed pallor, clubbing of the fingers, signs of mitral stenosis and insufficiency and palpable spleen. She had a leucocytosis. Four blood cultures were positive for *Streptococcus viridans*. She was given a trial of sulfadiazine; this caused a reduction in fever but blood cultures continued to be positive. She was then given a course of penicillin 200 000 units daily for 21 days. Blood cultures became negative and her fever subsided during that treatment, but she became progressively more decompensated and died in severe congestive failure on June 15 1944. Autopsy revealed healing vegetations on the mitral valve. The studies on her bacteremia reported here were done on Apr 19 1944.

Forty-eight specimens were obtained during a period of 49 minutes from the femoral artery, the renal and hepatic veins, and from the right auricle. The findings are presented in Table IX. When arterial and renal vein blood were compared the counts were found to be higher in arterial blood, although the differences were not great, venous figures being 73 to 99 per cent of the arterial levels.

In the next 8 pairs arterial and hepatic vein blood were examined. The counts in arterial blood during this time ranged between 188 and 288, while those in blood from the liver varied between 1 and 12. In every instance, therefore, the bacterial content of hepatic vein blood was less than 5 per cent of that of arterial blood.

The last 8 pairs in this study included arterial and right auricular blood. Arterial counts ranged from 250 to 322, while the mixed venous blood gave colony counts from 151 to 230. In individual pairs the venous counts were from 19 to 82 per cent of the corresponding arterial levels.

DISCUSSION

Previous to this there have been few investigations of the mechanism of removal of bacteria from the blood in human beings. Some workers have reported results of arterial and venous colony counts in the peripheral blood of patients with bacterial endocarditis, but these observations usually consisted of a single pair of samples from each patient (1, 5). Louroff has recently reported an investigation on a human being which he cites as evidence that the lungs remove bacteria from the blood in man (6). During an operation for ligation of an infected patent ductus arteriosus he took simultaneous cultures from the aorta and from the pulmonary artery. The aortic blood contained 51 colonies per cc., while the sample from the pulmonary artery contained "innumerable" colonies. Louroff offers this observation as proof that the lungs play an important part in the removal of bacteria from the blood. We are hesitant to accept such a conclusion, principally because it is based on a single pair of samples. The chance presence of an infected embolic particle in the blood from the pulmonary artery could account for the large number of colonies present in that blood, indeed, the very fact that "innumerable" colonies were found suggests that this may have been the case, since it is certainly uncommon to find so many colonies in the peripheral blood of a patient with left-sided endocarditis. Unfortunately, our own studies do not provide any information on the question of removal of bacteria by the lungs.

A considerable amount of work has been done on the mechanism of removal of bacteria from the circulating blood in experimental animals. The principal findings have been reviewed by Ottenberg (7). The results have not all been in agreement, but in the various experiments it appeared that organisms may be removed by the liver, the spleen, the bone marrow, the lungs, and the skeletal

muscles. Certain differences have been noted according to the kind of experimental animal, furthermore all bacteria do not appear to be disposed of in the same way. An important factor is the presence or absence of immunity to the infecting organisms. In that connection it should be stressed that the findings reported here apply to a disease in which a high degree of immunity to the infecting organism is nearly always present. In other types of bacteremia the pattern of disposal of bacteria may be somewhat different.

As would be expected in bacterial endocarditis, the colony counts in our patients were higher in arterial blood than in venous blood. That a considerable portion of the bacterial content of blood disappears during one circuit of the body is shown by the fact that mixed venous blood in the right auricle usually had a colony count only one half to two thirds as high as the corresponding arterial level. Possibly still further reduction takes place during passage through the lungs. In any event these studies indicate that a new supply of bacteria is constantly being added to the blood from the endocardial vegetations. An interesting feature of that replenishing is the fact that it appears to consist of a constant discharge of organisms and not a series of bacterial "showers." No doubt such "showers" may occur, but none happened to take place at the time of any of the numerous arterial cultures on these 6 patients. Instead, the arterial colony count maintained a remarkably constant level from minute to minute.

The most striking finding in this study was the small number of bacteria in blood obtained from the hepatic veins. In every one of the six patients a marked difference was found between arterial and hepatic vein colony counts, although the difference appeared to be proportionately greater in some than in others. In patients 1, 2, and 6 the colony counts in liver blood were less than 5 per cent of the arterial, while in patients 3 and 4 the difference was not quite so marked, and in patient 5 the reduction below the arterial level was only about half. It is perhaps relevant that the duration of illness was longest in patients 1, 2 and 6 and was shortest in patient 5. The efficiency of the removal mechanism may be influenced by patients' immunity to the infection.

Although it is true that some of the blood in the hepatic vein has previously passed through the capillaries of the spleen or the gastrointestinal tract, approximately 25 per cent of the blood supplied to the liver comes from the hepatic artery (8). It appears justifiable, therefore, to conclude that some bacteria are removed in the liver itself, since the removal of all bacteria which pass through the spleen, stomach, and intestines could not lower the colony count of blood in the hepatic vein by as much as 95 per cent.

The difference in bacterial content of blood from the antecubital and femoral veins is an interesting one. Femoral vein blood showed a fairly marked reduction below arterial blood, while antecubital vein blood was usually not much different from arterial blood. This difference between two peripheral veins is

probably referable to the character of the tissues drained by them. The antecubital vein drains blood principally from skin and superficial tissues. The circulation to the skin of the hands is unusual in that relatively little oxygen is extracted, indeed when the hands are warm much of the blood passes through special small arteriovenous shunts. It would seem that there is little opportunity for the removal of bacteria under these circumstances. The femoral vein, on the other hand, drains a large proportion of deeper tissues, muscles and bone marrow, both of which have been shown in experimental animals to be capable of removing bacteria from the circulating blood. From a practical standpoint, these studies indicate that there is little advantage to arterial, in preference to antecubital vein, cultures in routine clinical practice, since the number of organisms in antecubital vein blood is essentially the same as in arterial blood. It is conceivable, however, that if a patient were cold or emotionally disturbed, with vasoconstriction in the skin of the hands, the blood in the antecubital veins would contain fewer organisms since it would then consist of a greater proportion of blood which had passed through deeper tissues.

SUMMARY

In 6 patients with bacterial endocarditis studies were made of the bacterial content of arterial and venous blood. Paired samples were collected, approximately simultaneously, from two different locations in the circulatory system, and colony counts were determined. As many as 18 specimens were taken for culture during a single period of study. Venous blood was drawn not only from different locations in the extremities, but also from the superior and inferior venae cavae, the right auricle, and the hepatic and renal veins.

As would be expected, colony counts were highest in arterial blood.

Blood from the antecubital veins gave colony counts only slightly lower than arterial blood. In the femoral veins, on the other hand, there were appreciably fewer organisms. This difference is attributed to the type of tissues drained by the two veins.

Colony counts in blood from the superior and inferior venae cavae were also lower than arterial counts, the ratio being comparable to that found in femoral vein blood.

In the renal veins colony counts were only slightly below the arterial level indicating that few organisms are removed from the blood during passage through the kidneys.

The greatest reduction in bacterial content was found in hepatic vein blood. In 3 of the 6 subjects this reduction amounted to more than 95 per cent, and in all subjects the difference was very considerable.

Mixed venous blood in the right auricle of the heart gave colony counts which were usually one-half to two-thirds as high as in corresponding samples of arterial blood.

An interesting finding in these studies was a remarkable constancy of the bacterial content of arterial blood, during periods of 1 or 2 hours. Despite the fact that a considerable portion of the bacteria which leave the heart in arterial blood appear to be removed during a single circuit of the body, the number of bacteria in successive samples of arterial blood shows little change. This indicates that in bacterial endocarditis organisms are discharged into the blood from the endocardial vegetations at a comparatively even rate, rather than in a haphazard fashion as a result of the breaking off of infected particles.

This investigation was carried out with the technical assistance of Miss Med Scott Brown, Miss Elouse Cavin, Miss Elizabeth Roberts, and Miss Maurine Gliese.

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SUMMARY

In 6 patients with bacterial endocarditis studies were made of the bacterial content of arterial and venous blood. Paired samples were collected, approximately simultaneously, from two different locations in the circulatory system, and colony counts were determined. As many as 48 specimens were taken for culture during a single period of study. Venous blood was drawn not only from different locations in the extremities, but also from the superior and inferior venae cavae, the right auricle, and the hepatic and renal veins.

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Mixed venous blood in the right auricle of the heart gave colony counts which were usually one-half to two-thirds as high as in corresponding samples of arterial blood.

AN ETIOLOGIC CONSIDERATION OF DONOVANIA GRANULOMATIS CULTIVATED FROM GRANULOMA INGUINALE (THREE CASES) IN EMBRYONIC YOLK*

By KATHERINE ANDERSON PH.D. W. A. DEMONBREUN M.D., AND
E. W. GOODPASTURE, M.D.

(From the Department of Pathology, Vanderbilt University School of Medicine, Nashville)

PLATES 1 AND 2

(Received for publication September 5 1944)

The identification of the etiologic agent of granuloma inguinale has remained an unsolved problem since Donovan in 1905 described peculiar intracellular parasites as being consistently present in smears from the ulcerated lesions of this disease (1). Donovan himself was puzzled as to the exact nature of these intracellular bodies that bear his name but considered them to be protozoa. Donovan bodies are now generally accepted as being pathognomonic for granuloma inguinale and evidence has accumulated to support the hypothesis of their etiologic function (Figs. 1, 2). However, in spite of the efforts of many investigators, no microorganism acceptable as the etiologic agent of granuloma inguinale has been isolated and cultivated outside the human host.

Numerous investigators have cultivated various bacteria to which they attached etiologic significance (2-7). There has been no convincing consistency in the types of bacteria isolated by various workers beyond the fact that a majority of them seem to have been related to the Friedländer group. All the bacteria appear to have grown well on ordinary culture media; differential identification was based on variable cultural characteristics. A few attempts have been made to attach an etiologic significance to these bacteria by serological means (8, 9) but no experimental lesion comparable to that of granuloma inguinale has been induced by any of them.

The best experimental investigations directed toward a solution of the problem of etiology of granuloma inguinale led to conclusions that the Donovan body is the etiologic agent and that it has not as yet been cultivated outside the body of the human host (10). Recent experiments supporting these conclusions deserve some detailed consideration.

In 1931 DeMonbreun and Goodpasture aspirated material from two unruptured lesions in a negro man with other ulcerated lesions of granuloma inguinale. This material was especially rich in Donovan bodies and entirely free from contaminating microorganisms. From this inoculum the authors failed to cultivate the Donovan organism on any of a wide variety of media. Scrapings from ulcerated lesions, rich in Donovan bodies and with only slight contamination, failed to induce infection in guinea pigs, rabbits, kittens, dogs, and rats. An infection was established in monkeys by

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repeated injections of this especially good inoculum but the lesions healed without ulceration. These authors observed that the Donovan microorganism appeared to remain viable in uncontaminated human tissue for a considerable length of time. They concluded that the Donovan body is the etiologic agent of granuloma inguinale and judged that none of the microorganisms which had been reported as cultivated from human lesions was responsible for the disease (11).

More recently Dienst, Greenblatt, and Sanderson (12), and Greenblatt, Dienst, Pund, and Torpin (13) have recognized un ulcerated lesions in human patients which they called pseudobubos. From such lesions they, like DeMonbreun and Goodpasture, were able to aspirate material rich in Donovan bodies and entirely free from recognizable or cultivable contaminants. This material appeared to contain a pure culture of Donovan bodies. Neither contaminants nor Donovan microorganisms were cultivable on various artificial media, nor was this inoculum infectious for ordinary experimental animals, including the chorioallantois of chick embryos. They were able, however, to reproduce in four human volunteers experimental lesions acceptable both clinically and microscopically as granuloma inguinale. This series of experiments justifies the authors' conclusions that the Donovan body is the etiologic agent of granuloma inguinale, that it is not related to the Friedlander-*aerogenes* group of bacteria, and that it had not as yet been cultivated outside the human body. Carter, Jones, and Thomas (14) recognized Donovan bodies in pure culture in pseudobubos and likewise failed to cultivate them on ordinary culture media, in ordinary laboratory animals, or on the chorioallantois of chick embryos. They agreed with Greenblatt and his associates that the Donovan body is not cultivable on a wide variety of culture media known to be useful for the cultivation of certain fastidious microorganisms and that ordinary laboratory animals including the chorioallantois of chick embryos are not susceptible to infection by it.

In a previous report one of us described very briefly the successful cultivation in the yolk of living chick embryos of a microorganism having all the morphological characteristics of Donovan bodies (15). In the present paper we describe in greater detail our continued observations. The same microorganism has been isolated and cultivated from two additional cases of granuloma inguinale. It has been cultivated in the yolk of chick embryos inoculated with human tissue free from contamination but the cultured strains have not grown on any of a variety of ordinary culture media nor are they infectious for mice, dogs, chickens, rabbits, and monkeys. It does not grow on the chorioallantois of chick embryos. It appears, then, that the yolk of the intact, living chick embryo is a suitable and a very favorable medium for the cultivation of Donovan bodies. From this medium we are able to obtain the Donovan microorganism in quantity satisfactory for skin tests. We are also able to obtain a precipitable mucoid substance from infected yolk which gives a specific precipitation response with patients' serums and likewise elicits positive complement fixation reactions. The remainder of this report will describe in some detail the technique of isolation and cultivation of what we may call the Donovan microorganism. We will describe its variable morphology and its behavior

in embryonic yolk. An accompanying paper will describe something of its immunologic relations to patient's serum and skin reactions following intracutaneous injection of the bacterial cells and their products.

Technique of Isolation and Culture

The 3 cases from which the Donovan microorganism was cultivated were carefully selected. Successful cultivation of it by the technique to be described depends primarily upon its isolation from contaminants in fragments of infected human tissue, and subsequently upon its inoculation into the yolk of developing chick embryos.

Isolation of Strain I, Oct. 26, 1942—The first strain was isolated from a case of granuloma inguinale whose ulcerated lesion after removal of superficial exudate by swabbing with saline-soaked gauze sponges, yielded scrapings of tissue unusually rich in Donovan bodies and with minimal bacterial contamination as seen in smears stained by Wright's method.

Part of the lesion was again thoroughly swabbed with sterile saline. A small piece of tissue was clipped from the granulating surface with sharp scissors and placed between folds of moist gauze. With sterile spear-point dissecting needles part of the tissue was fragmented into bits 1 c. mm. or less in size. One or two fragments were smeared over the surface of 6 cystine agar slants. Bits of tissue were left on the slants which were incubated at 37°C.

The remaining fragments were ground with a pestle suspended in saline, and injected in progressive and arbitrary dilutions into the yolk of twenty-four 9-day-old chick embryos. The last embryo inoculated received extremely small amounts of the original tissue. A blood agar slant inoculated with 3 to 4 drops of the final dilution showed bacterial contamination.

All embryos were killed within 24 hours by an overwhelming growth of various bacterial contaminants. After 48 hours' incubation 4 cystine agar slants showed 1 to 4 staphylococcus colonies. Two were apparently free from contaminants. Smears from the latter stained by Gram's method showed small groups of Gram-negative bipolar rods resembling the non-encapsulated bacilli always associated with Donovan bodies in smears from human lesions. Wright's stain of a similar smear failed to demonstrate encapsulated microorganisms but confirmed the likeness of these forms to those of unencapsulated Donovan microorganisms. After 96 hours' incubation neither slant gave evidence of bacterial contamination and additional smears showed the continued presence of Gram-negative bacilli occurring in small groups in and about dead cells. They appeared to be viable by the quality of their staining reaction but one could not judge either grossly or microscopically that they were growing. Each apparently uncontaminated slant was washed with 3 cc. of saline; the washings were pooled and 0.5 to 1 cc. was inoculated into the yolk of six 8-day-old embryos. Subcultures from the original cystine agar slants to other cystine agar slants failed to give the slightest evidence of growth. On the 3rd day 2 embryos were dead without evidence of bacterial growth. Smears from the yolk of live embryos did not show evidence of bacterial growth.

On the 8th day smears from the yolk of the 4 living embryos stained with Wright's and Gram's stains revealed the presence in abundance of both encapsulated and non-encapsulated Gram-negative microorganisms indistinguishable from Donovan bodies and from those pleomorphic Gram-negative non-encapsulated forms always present in smears from lesions of granuloma inguinale (Fig. 4).

Infected yolk was drawn from each embryo. Parts of yolk sacs were ground, suspended in saline, and used as inoculum for various media and for embryos. Some yolk sac tissue was fixed in Zenker's fluid for histological sections. Additional 8-day-old embryos were inoculated with 0.5 cc. of infected yolk or suspended ground yolk sac.

may prolapse through the pylorus into the duodenum and produce a similar defect in the barium shadow (fig. 2). Eliason, Pendergrass and Wright²¹ have shown that when prolapsing gastric mucosa is accompanied by a prolapsing polyp or new growth two filling defects are produced, one in the bulb by the pedunculated tumor and another in the pylorus by the hypertrophied gastric mucosa. In these cases an important diagnostic point is the absence of the filling defect in a roentgenogram made with the patient in the erect position and the presence of the defect in one made with the patient in the prone position.

In differentiating a benign tumor from an ulcer, it should be remembered that an ulcer does not produce a central filling defect. The niche

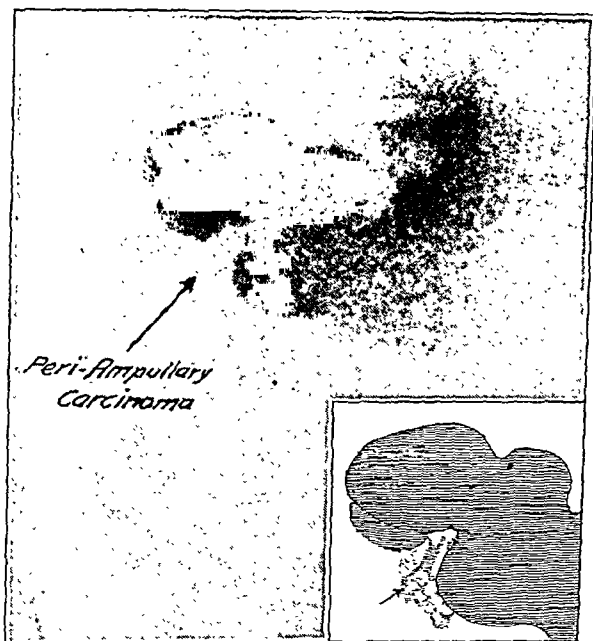


Fig. 19 (case 10).—Carcinoma of the periampullary portion of the duodenum. The stomach was not dilated, and there was active peristalsis. The first portion of the duodenum was obscured by the antrum of the stomach. There were irregularity, narrowing and deformity of the descending portion of the duodenum.

produces a constant disturbance in the outline of the bulb and may be associated with an incisura. The usual finding is hyperperistalsis with delay in motility. Adhesions usually produce an irregularity of the outline of the bulb, with fixation, gastric hyperperistalsis and delayed motility.

A tumor in the region of the pancreas, pressing on the barium-filled lumen, may produce a central translucency of intraluminal growths,

21. Eliason, E. L.; Pendergrass, E. P., and Wright, V. W. M.: Roentgen Ray Diagnosis of Pedunculated Growths and Gastric Mucosa Prolapsing Through the Pylorus, *Am. J. Roentgenol.* **15**:295, 1926.

but it is exceptional to have the defect confined to the cap and remain constant in all the horizontal positions (Shiflett ²²).

Diverticulum of the duodenum is not an exceptionally rare finding. Ritchie and McWhorter ²³ collected reports of 76 cases from the literature, and Morrison and Feldman ²⁴ reported 12 personal cases, in 1 of which a carcinoma developed. The best method of recognizing a diverticulum is fluoroscopy, during which the examiner can, by manipulation, cause the pouch to fill and empty. The appearance is characteristic, with regular and smooth outlines. When the ostium of the diverticulum

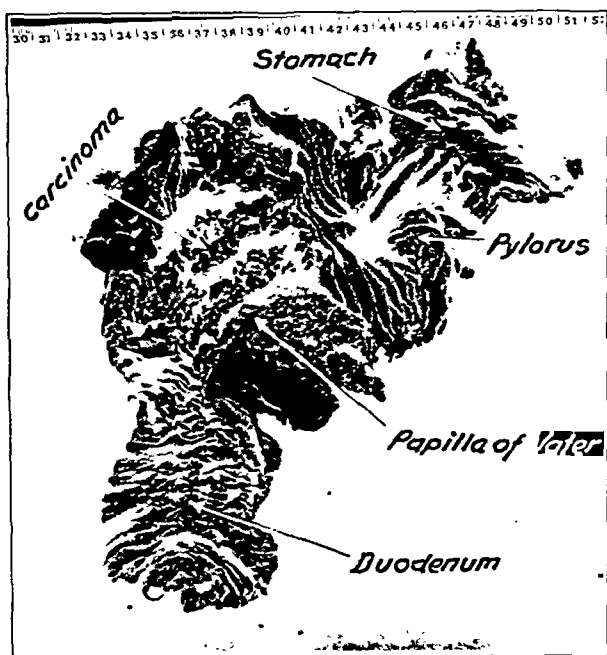


Fig. 20 (case 10).—Photograph of the gross specimen of a carcinoma of the periampullary portion of the duodenum demonstrated in figure 19.

is small, the barium may be retained in a diverticulum for as long as fifty-two days (LeWald ²⁵). The importance of diverticulum in con-

22. Shiflett, E. L.: Tumors of the Duodenum and Hypertrophied Gastric Mucosa Prolapsing Through the Pyloric Canal into the Duodenum, *Radiology* **19**:79, 1932.

23. Ritchie, H. P., and McWhorter, G. L.: Duodenal Diverticula, *Surg., Gynec. & Obst.* **25**:485, 1917.

24. Morrison, T. H., and Feldman, M.: A Case of Carcinoma in a Duodenal Diverticulum with a Consideration of Duodenal Diverticulosis, *Ann. Clin. Med.* **4**:403 (Nov.) 1925; Autopsy Report of a Case of Primary Carcinoma in a Duodenal Diverticulum, *ibid.* **5**:326, 1926.

25. LeWald, L. T.: Right-Sided Diverticulitis and Diverticulosis, *Radiology* **4**:1 (Jan.) 1925.

nection with carcinoma of the duodenum is twofold: First, carcinoma may arise in a diverticulum (Morrison and Feldman²⁴) and, second, the crater of an ulcerated carcinoma may duplicate the roentgenographic appearance of a diverticulum, as occurred in case 12 of our series (figs. 21, 22 and 23).

The difficulties encountered and the errors made in the roentgen examination in cases of cancer of the duodenum are illustrated by the record of this series. Of the 18 cases reported here, roentgenograms of the gastro-intestinal tract were made in 16. The results are shown in table 2. From a study of this it is seen that in the 3 cases in which the lesion was located above the ampulla definite abnormalities were



Fig. 21 (case 12).—Carcinoma of the periampullary portion of the duodenum simulating a diverticulum. Note the prominent duodenal bulb and what appears to be a diverticulum of the first portion of the duodenum. At operation this proved to be the crater in an ulcerated carcinoma of the periampullary portion of the duodenum.

noted. The diagnosis of a malignant growth was made in 1 case and suggested as a possibility in another. In only 1 case was a malignant tumor of the duodenum suspected. The diagnoses were "carcinoma of the pylorus," "obstruction of the duodenum, possibly malignant," and "pyloric obstruction." In 7 of the 9 cases of carcinoma in the periampullary portion of the duodenum, roentgenographic studies of the gastro-intestinal tract were made. The diagnoses were, respectively, "carcinoma of the head of the pancreas," "negative" (2 cases), "per-

forating ulcer," "diverticulum," "obstruction of the second portion of the duodenum" and "biliary obstruction with deformity of duodenum, probably from adhesions." In 6 cases of carcinoma of the infra-ampullary portion the diagnosis was, respectively, "carcinoma of the head of the pancreas," "negative," "duodenal obstruction, probably due to adhesions, but pancreas may be involved" and "deformity and narrowing of duodenum" and (in the 2 remaining cases) "duodenal obstruction."

Here, then, are the diagnoses, made by 6 roentgenologists based on the roentgen examinations in 16 cases in which clinical symptoms were

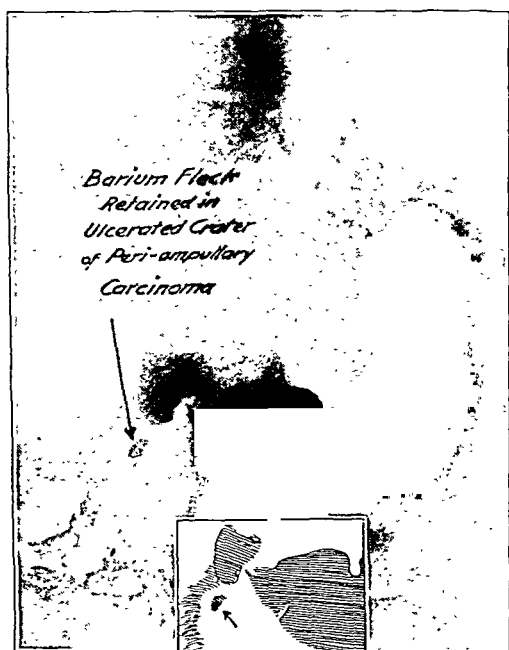


Fig. 22 (case 12).—Roentgenogram of the carcinoma demonstrated in figure 21. Note the barium retained in the crater of the ulcerated carcinoma.

present. In all but 1 of them obvious pathologic changes were evident on the films, yet in only 1 instance was the possibility of a primary carcinoma of the duodenum suggested. In 14 instances, however, the abnormal findings were recognized and described. The conclusions which seem to be justified are: The diagnosis of carcinoma of the duodenum occasionally will be made from the roentgen picture alone, but in most cases a careful correlation and synthesis of the evidence and information derived from all possible methods of clinical investigation are necessary.



Fig. 23 (case 12).—Roentgenogram of the carcinoma demonstrated in figure 21. Note the barium retained in the crater for twenty-four hours.

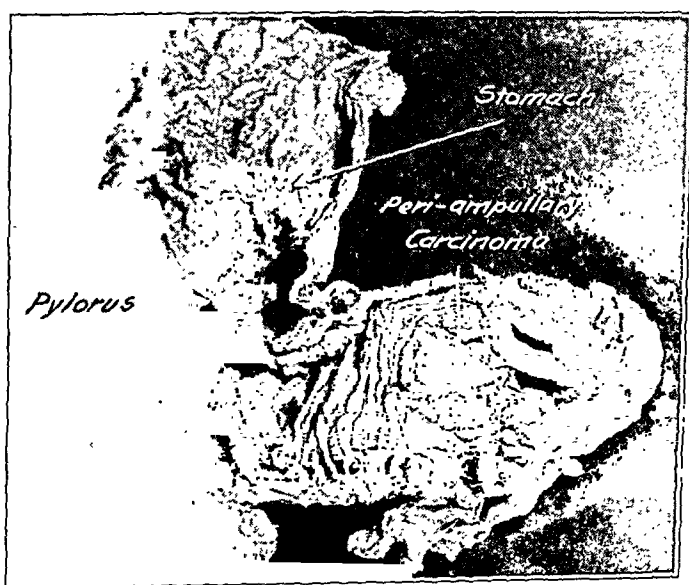


Fig. 24 (case 12).—Gross specimen of the carcinoma shown in figure 21.

DIAGNOSIS

The diagnosis of cancer of the duodenum is attended with so much difficulty that most of the recorded cases were recognized only at operation or at autopsy. In only a few cases reported in the literature

TABLE 2.—*Summary of Roentgen Findings and Diagnosis*

Patient	Location of Growth	Roentgen Findings	Roentgen Diagnosis
M. B.	Supra-ampullary	Dilated pylorus; deformed duodenum distal to cap	Carcinoma of pylorus
D. H.	Infra-ampullary	Deformity of duodenal cap; widening of duodenal loop	Carcinoma of head of pancreas
B. K.	Periampullary	Infiltration of duodenum; gastric retention; enlarged gallbladder	Carcinoma of head of pancreas
C. S.	Periampullary	Hypomotility; large duodenal cap; irregular outline of second portion, partial obstruction of duodenum	No pathologic process
H. S.	Supra-ampullary	Filling defect in junction of first and second portions of duodenum with obstruction and retention	Inclined to think growth benign but must consider possibility of malignancy
L. H.	Supra-ampullary	Almost complete "pyloric obstruction with retention of 90% of barium at 6 hr."	Pyloric obstruction
M. B.	Infra-ampullary	No evidence of cancer or ulcer; no obstruction or dilatation	No evidence of cancer or ulcer in either stomach or duodenal cap; no obstruction or dilatation
H. B.	Infra-ampullary	Obstruction of second and fourth portions of duodenum with gastric retention	Obstruction, probably due to adhesions, but pancreas may be involved
A. B.	Intra-ampullary	Stomach not dilated; active peristalsis; first portion of duodenum obscured by antrum of stomach; irregularity, deformity and narrowing of descending portion of duodenum	No definite diagnosis made
S. A.	Periampullary	Duodenal outline irregular and curves far out to right; 6 hr. retention in stomach; ulcer crater in second portion of duodenum; gallbladder enlarged	Perforating ulcer
J. R.	Infra-ampullary	Obstruction of third portion of duodenum; marked dilatation of entire duodenum and retention of barium	Obstruction of duodenum
W. F.	Infra-ampullary	Obstruction of third portion of duodenum; moderate retention of barium in terminal portion of duodenum; no dilatation	No diagnosis made
F. K.	Periampullary	No roentgenograms of gastro-intestinal tract made; injection of biliary tract through gallbladder drain showed dilatation of biliary duct system and obstruction of common duct at ampulla	Dilatation of bile duct
A. B.	Periampullary	Distended gallbladder; irregularity and deformity of second portion of duodenum; no gastric retention	Biliary obstruction; deformity of duodenum probably the result of adhesions
G. B.	Periampullary	Obstruction of second portion of duodenum	Obstruction of second portion of duodenum
C. G.	Periampullary	No evidence of pathologic process in stomach or duodenum (studies made twelve months before admission to hospital)	No evidence of pathologic process in stomach or duodenum

has the condition even been suspected. Because of its rarity, it is usually not even considered as a possibility in the differential diagnosis. A further explanation is the fact that cancer of the duodenum is usually mistaken for other lesions of the upper portion of the abdomen. Nevertheless, if the possibility of carcinoma of the duodenum is given

consideration, it should be feasible to make a presumptive diagnosis in certain of these cases. In the early stage, however, symptoms are so few that such a hope is probably not justified, and the diagnosis must await exploratory operation.

The presenting symptoms of cancer of the duodenum usually are epigastric pain and obstruction of the upper part of the intestinal tract,



Fig. 25 (case 12).—Microscopic section of the adenocarcinoma shown in figure 21.

with or without biliary obstruction and jaundice. The logical sequence of procedure, naturally, is to locate the level of the obstruction definitely and finally to determine its cause. The indication that the level of the obstruction is in the stomach, duodenum or upper part of the jejunum

is furnished by the presence of gastric retention and dilatation, the absence of intestinal contents in the vomitus and the flat or sunken abdomen without gaseous distention. The commonest obstructive lesion in this region is a carcinoma of the pylorus. This can be ruled out by the roentgen examination revealing a normal gastric outline and motility and a patent or even dilated pylorus. Should the gastric analysis disclose normal free hydrochloric acid, it will help exclude the stomach as the primary site; if diminished or absent, it will not be conclusive.

If bile and pancreatic juice are not found in the vomitus and there is no evidence of jaundice, the point of the obstruction will be in the supra-ampullary portion of the duodenum. The presence of biliary obstruction and jaundice definitely locates the obstruction in the neighborhood of the ampulla, and roentgenograms may show a dilated first portion of the duodenum above an irregular constriction, a gaping

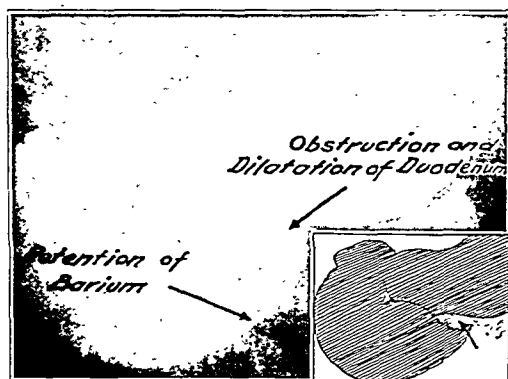


Fig. 26 (case 13).—Obstruction of the third portion of the duodenum with dilatation and retention of barium in the stomach and duodenum after six hours.

pylorus, distended stomach and retention of barium after six hours (figs. 19 and 27). Obstruction of the jejunum can be ruled out by the absence of intestinal contents in the vomitus and by roentgen studies. If the roentgenogram reveals a long, dilated proximal portion of the duodenum above a point of obstruction, with or without irregularity of the duodenal lumen, it is fair to assume that the lesion is in the third portion of the duodenum (fig. 26). When the lesion is below the ampulla of Vater, bile and pancreatic juice are usually found in the gastric contents on repeated examinations, as Mateer and Hartman¹⁸ and others have emphasized.

Even after the level of obstruction has been determined or assumed, a definite diagnosis of cancer of the duodenum cannot be made until other nonmalignant causes of obstruction have been eliminated. The commonest cause of obstruction of the first portion of the duodenum

is constriction by scars of a chronic duodenal ulcer. Evidence against such a cause and in favor of a malignant growth would be the lack of any characteristic history of ulcer, the more rapid development of emaciation, cachexia and stenosis, a marked decrease or absence of free hydrochloric acid, the presence of a palpable tumor and the failure to demonstrate an ulcer by roentgen examination (Eger¹⁶).

Of all causes of obstruction of the supra-ampullary portion of the duodenum by external pressure mentioned by various authors, enlargement of the gallbladder is, perhaps, the most frequent. Others are: tumors of the omentum, kidney, pancreas and liver, enlarged retro-peritoneal glands and an aneurysm of the celiac axis or of the hepatic

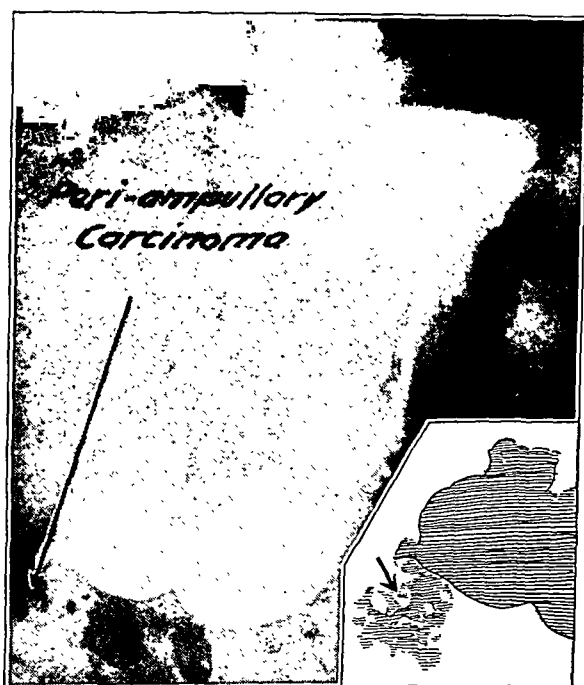


Fig. 27 (case 16).—Carcinoma of the periampullary portion of the duodenum. Note the irregularity and deformity of the second portion of the duodenum.

artery (Fenwick²⁶). In differentiating these from cancer of the duodenum, the greatest weight must be given to the following findings, which are common in association with cancer of the duodenum and rare with these other conditions: a severe degree of obstruction of short duration and rapid development, marked cachexia and loss of weight, the presence of blood in the vomitus and stools and marked decrease or absence of free hydrochloric acid in the gastric secretion. Additional aid may be afforded by roentgenographic study of the gallbladder, although it must be remembered that this organ is usually enlarged

26. Fenwick, W. S.: Primary Carcinoma of the Duodenum, *Edinburgh M. J.* 10:309, 1901.

whenever biliary obstruction is produced by a malignant tumor, whether the primary site is the common duct, ampulla, papilla, head of the pancreas or duodenum.

Cancer of the periampullary portion of the duodenum, therefore, is even more difficult to differentiate from obstruction due to other causes. Acute pancreatitis usually has an explosively swift onset, with violent pain and without actual obstruction of the duodenum or alteration in the quantity of free hydrochloric acid in the gastric secretions. Chronic pancreatitis and carcinoma of the head of the pancreas are not likely to cause obstruction of the duodenum or produce blood in the stools or vomitus or cause any reduction in free hydrochloric acid. Cancer of the bile duct, ampulla or papilla causes jaundice of a rapidly progressive unremitting, obstructive type, without symptoms or signs by which it can be differentiated prior to operation or autopsy.

Cancer of the infra-ampullary portion of the duodenum is usually an extensive tumor, often bulky and frequently located immediately proximal to the ligament of Treitz (fig. 26). It, therefore, often may furnish adequate roentgen signs by which the location and extent of the involvement may be fairly well indicated. The differentiation of an obstruction at this level from one in the supra-ampullary portion may be aided by the consistent finding of bile and pancreatic juice in the gastric contents. Other causes of obstruction in the infra-ampullary portion, such as enlargement of the retroperitoneal nodes, retroperitoneal tumor, pressure by superior mesenteric vessels, impaction of a large gallstone in the duodenum and external pressure from a tumor of a contiguous viscus such as the pancreas, must be considered (Eger¹⁶).

The difficulty of diagnosing cancer of the duodenum is illustrated by the records of this series of 18 cases. Although we have personally examined and studied 5 patients, in only 1 instance was the suggestion made that the lesion might be a primary carcinoma of the duodenum.

TREATMENT

Study of any large series of cases of duodenal carcinoma will reveal two outstanding facts: (1) In a large percentage of cases no evidence of metastasis or local extension of the disease is found at operation, and (2) a high mortality accompanies operative attempts at cure. The first point suggests that successful surgical removal of all the malignant disease might often be feasible if this mortality could be brought down to a reasonable level. The reason for the high mortality is obvious. Not only are the surgical procedures of unusual magnitude, but they must be carried out on patients who often are already moribund from the effects of interference with vital processes. Most of these patients have symptoms of high intestinal obstruction, often complicated by

TABLE 3.—Summary of Diagnostic Data

	Origin in Duode- num*	Sex	Age, Years	Duration of Symptoms	Pain in Right Upper Quadrant and Epi- gastric Distress	Vomit- ing	Jaun- dice	Fever and Evidence of Sepsis	Loss of Weight	Palpable Mass in Epi- gastrium	Pal- pable Edge of Liver	Occult Blood in Stools	Bile in Stools
Case 1.....	Supra	F.	48	4 mo.	Yes	No	No	No	Yes	Yes, 5 cm., movable	No	No	Yes
Case 2.....	Infra	F.	28	6 mo.	Yes	Yes	No	No	Yes	Yes, 12 cm., fixed	No	—†	—
Case 3.....	Peri	F.	60	3 mo.	Yes	No	No	No	Yes; emaciated	Yes, 10 cm., movable	No	—	—
Case 4.....	Peri	F.	47	2 mo.	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No; clay colored
Case 5.....	Supra	F.	68	9 mo.	Yes	Yes	No	No	Yes; 20 lb.	Yes	Yes	No	Yes
Case 6.....	Supra	F.	70	5 wk.	Yes	Yes	No	Yes	Yes; emaciated	No	No	No	Yes
Case 7.....	Infra	F.	51	10 mo.	Yes	Yes	Yes	No	Yes; 40 lb.	No	No
Case 8.....	Peri	F.	52	6 wk.	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No
Case 9.....	Infra	M.	78	6 mo.	Yes	Yes	No	No	Yes; 25 lb. in 6 wk.	Yes	No	—	—
Case 10.....	Infra	M.	71	1 yr.	No	No	No	No	No	No	No	No	No
Case 11.....	Peri	M.	18	1 yr.	Yes	No	Yes	No	Yes	Yes; 8 cm. in diameter; moderately movable	No	—	No
Case 12.....	Peri	F.	56	2 mo.	Yes	No	Yes	Yes	Yes	Yes; definite mass	No	No	No; pale
Case 13.....	Infra	M.	51	2 yr.; gastric distress	Yes	Yes	No	No	30 lb. in 6 wk.	No
Case 14.....	Infra	M.	?	Yes	...	No	No	Yes	Yes
Case 15.....	Peri	F.	36	2 mo.	Yes	Yes	Yes	Yes	Yes; extreme loss	No	Yes	No	No
Case 16.....	Peri	M.	58	6 wk.	Yes	No	Yes	Yes	Yes	No	No	No	No; pale
Case 17.....	Peri	F.	45	6 wk.	Yes	Yes	No	No	Yes	Yes	No	No	Yes
Case 18.....	Peri	F.	45	1 yr.	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No

of Primary Carcinoma of the Duodenum

Bile in Urine	Biliary Drainage, Bile Obtained	Icteric Index	Gastric Analysis	Roentgen Picture with Barium Meal	Course
No	—	—	Normal	Dilated pylorus; deformed duodenum distal to cap	Died 8 days after gastroenterostomy of acute surgical parotitis (bilateral)
No	—	—	—	Deformity of duodenal cap; widened loop	Exploratory laparotomy showed mass thought to be retroperitoneal sarcoma; after 12 roentgen treatments mass regressed; after 6 mo. recurred; radium pack treatments ineffectual; laparotomy and implantation of radon seeds; died 4 days later
No	—	—	—	Pressure defect of greater curvature of stomach; infiltration of duodenum; gastric retention after 6 hours; enlarged liver shadow	Exploratory laparotomy; death from peritonitis
Yes	—	—	—	Dilated first portion of duodenum with irregular outline of second portion and partial obstruction	Rapid downhill course, patient vomiting large amounts of bile-stained fluid; death 33 days later
—	—	—	—	Persistent filling defect of junction of first and second portions of duodenum with obstruction and 48 hours gastric retention	Posterior gastro-enterostomy for cancer of duodenum causing obstruction, involving the first and second parts of duodenum; tumor hard and elastic and obviously malignant; no metastases; no biopsy
—	—	—	—	Almost complete pyloric obstruction with 80% retention at 6 hours	Death 3 days after admission due to myocardial failure
Yes	—	Increased	—	Involvement of duodenojejunal junction by irregular mass causing partial obstruction	Rapid downhill course; stercoraceous vomiting and death in 3 days
Yes	—	Increased	—	Rapid decline; death week after admission
No	—	Normal	—	Obstruction of second and fourth portions of duodenum with gastric retention	Anterior gastro-enterostomy and enterostomy; death 8 days later due to peritonitis
No	—	Normal	—	Dilatation of duodenal cap and first portion; second portion irregularly narrowed and deformed; no diagnosis made	Steady downhill course; death 3 months later
No	—	Increased	Normal	Duodenal outline irregular and curves far out to right; 6 hour retention in stomach; ulcer crater in lower part of second portion of duodenum; gallbladder shadow enlarged	Untraced
No	—	35	—	Shadow of duodenal cap large; second portion narrowed; barium retained in crater in second portion after 24 hours; considered to be diverticulum	Exploratory laparotomy; tumor of second portion of duodenum found and exposed by duodenostomy; distended gallbladder drained by cholecystostomy; death 7 days later due to bronchopneumonia
...	Obstruction of terminal portion of duodenum; dilatation of duodenum; 6 hour retention of barium	Lived 2 years
...	Obstruction of terminal portion of duodenum; small retention; no dilatation	Untraced
Yes	..	100	..	No gastric studies made; dilated bile ducts shown by injection through gallbladder drainage tube	Downhill course; death 4 months after admission
Yes	—	?	—	Irregularity and deformity of second portion of duodenum; gallbladder distended	Exploratory operation; obstruction of common duct; no stone found; T tube inserted; biliary obstruction relieved; hemorrhage from wound 4 weeks later; duodenum exposed and carcinoma excised; death 6 hours later
No	—	—	—	Obstruction of second portion of duodenum with marked dilatation of duodenum and gastric residue	Posterior gastro-enterostomy and cholecystogastrostomy; recovery; lived 2 years
Yes	Slight amount of bile obtained	133	Normal	Negative (12 months before admission)	Steady downhill course for 1 year terminated by massive hemorrhage from duodenal tumor

* Supra refers to the supra-ampullary portion of the duodenum; infra, to the infra-ampullary portion, and peri, to the peri-ampullary portion.

† The dash indicates that this part of the examination was omitted in this case.

biliary obstruction and chronic hemorrhage. They commonly show advanced degrees of starvation, dehydration, acidosis, anemia, jaundice and gastric distention. A high mortality cannot be avoided if such patients are operated on without adequate preparation.

The dehydration should be corrected by the daily administration of from 3,000 to 5,000 cc. of fluids by all routes. At least from 1,000 to 2,000 cc. of 1 per cent solution of sodium chloride and 10 per cent dextrose should be given intravenously daily. The stomach should be washed out at least once a day. Studies of the blood chemistry will indicate the progress of the patient. The anemia must be corrected by frequent transfusions, preferably of whole blood, which provides ideal nourishment and stimulation to these prostrated patients.

With jaundice present, the danger of hemorrhage increases. Even though jaundice may not be clinically evident, the amount of circulating bilirubin may, nevertheless, increase 800 to 1,000 per cent. The van den Bergh test, determination of the icteric index and estimation of the bleeding and the coagulation time furnish important information. Patients with jaundice should be prepared for operation by restoring the supply of calcium, sodium chloride, water and especially carbohydrates. Walters²⁷ recommended the administration of 5 cc. of a 10 per cent solution of calcium chloride intravenously for three days; 100 grains (6.5 Gm.) of calcium lactate by mouth daily for four days, and 4,000 cc. of water by all available avenues. In addition, proctoclysis of from 3 to 15 per cent dextrose solution is suggested. A 10 per cent solution of dextrose intravenously is the most direct way of supplying the carbohydrate which is almost a specific for hepatic insufficiency. With such a preparatory regimen, including blood transfusions, Walters²⁷ was able to reduce the coagulation time from fourteen to two minutes.

OPERATIVE PROCEDURES

The surgical procedures for the treatment of cancer of the duodenum are of two general classes: curative and palliative. In the first group the procedure must be varied according to the location and extent of the growth and the complications which accompany it. Rarely the primary growth may be so small that a simple excision may be sufficient (fig. 3). In the usual case, however, the growth involves so much of the lumen of the duodenum that a resection of the whole segment must be done. If the tumor is in the supra-ampullary portion, well above the bile and pancreatic ducts, this procedure plus posterior gastroenterostomy should be sufficient (fig. 4).

27. Walters, Waltman: Obstructive Jaundice: Its Surgical Aspects, *Ann. Surg.* 93:1137 (April) 1931.

Carcinoma of the periampullary portion, accompanied by biliary obstruction, entails radical excision of the affected segment, and, if possible, reimplantation of the common bile duct and the duct of Wirsung into the duodenum (fig. 5). When this is done, Cohen and Colp^s recommended that some operation be done to provide drainage of the gallbladder and thus take the strain off the newly implanted bile duct. The operations which may be employed are choledochostomy, cholecystostomy and cholecystenterostomy. Despite the fact that the addition of this procedure increases the mortality slightly, its advantages deserve consideration. Tension is certainly taken off the suture line, the flow of bile is assured, and should stricture or local recurrence develop, as happened in the cases of Mayo²⁸ and Rixford,²⁹ a second operation would not be necessary (Cohen and Colp^s).

If simple excision of the tumor of the periampullary region (fig. 3) is not sufficiently radical to get beyond the growth, it may be necessary to perform a circular resection of the duodenum, combined with partial pancreatectomy (fig. 4). Cohen and Colp reviewed the literature up to 1927 and found only 4 instances in which the patients had survived this formidable procedure. These were the celebrated cases of Halsted,²⁸ Kausch,³⁰ Hirschel³¹ and Tenani.³²

Halsted in 1898 resected a portion of the duodenum, restored its continuity by an end to end anastomosis, reimplanted the bile and pancreatic ducts and established a cholecystostomy stoma. Three months later cholecystoduodenostomy was performed. Kausch did a preliminary cholecystojejunostomy, and two months later resected the duodenum and part of the pancreas and performed pancreaticoduodenostomy and gastro-enterostomy. Tenani, more recently, at his first operation, did an exploratory duodenotomy, followed by posterior gastro-enterostomy, and after dividing the bile duct, he implanted the proximal end into the efferent duodenal segment. He then sutured the duodenum and closed the abdomen without drainage. One month later he resected the second portion of the duodenum and the involved portion of the head of the pancreas. The pancreatic stump was sutured into the efferent duodenal segment (fig. 3).

28. Cited by Upcott, H.: Tumors of the Ampulla of Vater, with a Report of Two Cases, *Ann. Surg.* **56**:710, 1912.

29. Rixford, cited by Outerbridge.¹⁴

30. Kausch, W.: Das Carcinom der Papilla duodeni und seine radikale Entfernung, *Beitr. z. klin. Chir.* **78**:439, 1912.

31. Hirschel, cited by Pallin, G.: Carcinom des Ductus hepaticocholedochus und seine chirurgische Behandlung (52 schwedische Fälle), *Beitr. z. klin. Chir.* **121**:84, 1920.

32. Tenani, O.: Surgery of the Papilla of Vater. *Policlinico (sez. chir.)* **22**: 291, 1922.

Hirschel performed circular resection of the duodenum with end to end suture, choledochoduodenostomy with a tube, resection of a part of the pancreas and pancreaticoduodenostomy and gastro-enterostomy. This extensive procedure was accomplished in the remarkable time of one hour. Since few surgeons could hope to equal this feat, one must agree with Cohen and Colp, from whose paper this material was reviewed, that it would be more practical to perform this operation in two stages, the first of which should be a drainage operation to eliminate the biliary obstruction and thus to get the patient into the proper physical condition to withstand the more exhausting second operation.

The fact that there are only 4 recorded cases in which reimplantation of the head of the pancreas or duct was successfully carried out after resection of the second portion of the duodenum would indicate the extreme hazard of this operation. According to Whipple, Parsons and Mullins,³³ two factors have been responsible for the mortality:

The first was the mistaken belief that the flow of pancreatic juice is essential to life. This had led surgeons to attempt to reestablish this flow into the duodenum or jejunum by implanting the resected head of the pancreas or the cut end of the duct into the upper intestine. The activation of the pancreatic ferments by duodenal contents compromised any type of anastomosis in the human subject, especially around the posterior aspect of the duodenum devoid of peritoneum. . . . The second factor was the attempt to carry out the excision of these tumors in one stage. . . .

The technic which they have evolved in their experience with 3 cases of carcinoma of the ampulla embodies the following principles: (1) resection of the descending loop of the duodenum with the pancreas wide of the growth, with no attempt to reestablish the continuity of the duodenum or of the pancreas with the intestine, and (2) division of the operation into two stages. At the first stage, posterior gastro-enterostomy is performed, the common duct is ligated and sectioned below the cystic duct and a cholecystogastrostomy stoma is made in the anterior surface of the stomach, well away from the pylorus, an anastomotic opening at least 2 cm. in diameter being used in order to avoid subsequent stenosis and cholangitis. At the second stage the descending portion of the duodenum is resected with inversion of the upper and lower ends, and a V-shaped portion of the head of the pancreas is resected together with the common duct. The pancreatic ducts are divided and ligated, and the cut surfaces of the pancreas are carefully approximated. Whipple, Parsons and Mullins have carried out this procedure on 3 patients. The first patient died eight months after the radical operation, following a sequence of events which included stenosis

33. Whipple, A. O.; Parsons, W. B., and Mullins, C. R.: Treatment of Carcinoma of the Ampulla of Vater, *Ann. Surg.* **102**:763. 1935.

of the cholecystogastrostomy opening, biliary stasis, infection and septicemia. The other 2 patients suffered no disturbance due to lack of pancreatic ferments. The utilization and absorption of fat in both cases were from 85 to 90 per cent, and the patients regained and maintained their normal weight three and seven months after operation.

Carcinoma of the infra-ampullary portion arises most often close to the duodenojejunal junction. This localization requires resection of the affected segment and reestablishment of the continuity of the intestine by end to end anastomosis or by duodenojejunostomy. End to end anastomosis is often impossible because of the necessity of resecting such a large extent of the duodenum that the ends cannot be approximated (fig. 5). The hazards of this operation are further increased by reason of the edema, hypertrophy and dilatation of the duodenal segment above the obstruction. The marked difference in the caliber of the two segments, the shrinkage of the proximal segment after relief of the obstruction and the strain caused by the rapid peristalsis of this region all increase the danger of leakage at the suture line. In this situation a side to side union, if anatomically feasible, is to be preferred.

In a somewhat analogous situation, Carter³⁴ resected a carcinoma of the jejunum located 6 inches (15 cm.) below the ligament of Treitz and performed a side to side duodenojejunostomy. He incised the anterior leaf of the transverse mesocolon and swung the distal portion of the jejunum to the right, contraclockwise, to lie beside the terminal portion of the duodenum, which was brought down through a slit in the mesocolon. He then completed a side to side anastomosis (fig. 5). Where so much of the duodenum has been resected that no form of duodenojejunostomy is possible, one must be content with gastro-enterostomy. This procedure, of course, is followed by regurgitation of bile and pancreatic juice into the stomach, and nausea and discomfort may be troublesome unless the stomach is thoroughly washed out daily.

PALLIATIVE OPERATIONS

Palliative operations are distinctly worth while in cases of inoperable cancer. Not only do they prolong life, but they spare the patient the suffering which precedes death by duodenal or biliary obstruction. Patients with inoperable carcinoma of the supra-ampullary portion of the duodenum may be greatly relieved by gastro-enterostomy, with or without an exclusion of the pylorus. Inoperable cancer of the peri-ampullary portion requires gastro-enterostomy and cholecystogastrostomy, cholecystoduodenostomy, cholecystenterostomy or cholecystostomy. Cancer of the infra-ampullary portion, accompanied by obstruction, may require cholecystogastrostomy and gastro-enterostomy.

34. Carter, R. F.: Carcinoma of the Jejunum, *Ann. Surg.* **102**:1019, 1935.

IRRADIATION FOR CANCER OF THE DUODENUM

Irradiation has not played a prominent part in the treatment of duodenal carcinoma. Most of the tumors are of the adult, differentiated type and not likely to respond to any dose of external radiation which can be tolerated by the overlying skin. Rarely an anaplastic tumor is encountered (as in our case 2), which may temporarily respond to external radiation. The literature contains reports of a few cases in which the surgeon at the time of operation placed radium capsules in the end of a duodenal tube introduced into the duodenum by way of the mouth, so as to lie in contact with the lesion for several hours and

TABLE 4.—*Operative Results*

Patient	Location of Growth	Hospital	Operation	Result
M. B.	Supra-ampullary	Memorial	Posterior gastro-enterostomy	Death due to bilateral surgical parotitis 4 days later
D. H.	Infra-ampullary	Memorial	Exploratory laparotomy and insertion of gold radon seeds	Death 4 days later
B. K.	Periampullary	Memorial	Exploratory laparotomy, duodenotomy and biopsy	Death 11 days later; fecal fistula, peritonitis and bronchopneumonia
S. A.	Periampullary	Post-Graduate	Biopsy, posterior gastro-enterostomy and cholecystogastrostomy	Recovery; patient untraced later
J. R.	Infra-ampullary	Post-Graduate	Gastro-enterostomy	Recovery; patient untraced later
W. F.	Infra-ampullary	Post-Graduate	Jejunostomy	Death 12 days later
G. B.	Infra-ampullary	Post-Graduate	Cholecystogastrostomy and gastro-enterostomy	Recovery; lived 2 yr.
H. S.	Supra-ampullary	Lenox Hill	Posterior gastro-enterostomy	Recovery; patient untraced
A. B.	Periampullary	Lenox Hill	Cholecystostomy, first stage; duodenotomy and excision of tumor at second stage	Death 6 hr. later
H. B.	Infra-ampullary	Polyclinic	Anterior gastro-enterostomy	Leakage at suture line; death due to peritonitis
E. D.	Periampullary	St. John's, Long Island City	Cholecystostomy, duodenotomy and biopsy	Death 3 days later due to bronchopneumonia
F. K.	Periampullary	New Haven, New Haven, Conn.	Cholecystostomy and duodenotomy and biopsy	Recovery; death 14 wk. later

later be withdrawn. Gold radon seeds have occasionally been inserted into the primary tumor (case 2). None of these procedures have been of much benefit, while the hazards of duodenal fistula, peritonitis and acute pancreatitis are great.

OPERATIVE RESULTS

Operation was performed in 12 of the 18 cases of carcinoma of the duodenum in this series. In only 1 was it possible to attempt to remove the growth. In this instance (case 16) cholecystostomy was performed as a first stage operation. At the second stage, the duodenum was opened, and a small periampullary carcinoma was excised. Death occurred six hours later.

Gold radon seeds were inserted into 1 inoperable tumor (case 2), which had previously undergone marked regression after roentgen therapy. The patient died four days later.

There were 5 postoperative recoveries (41.6 per cent). The location of the tumor and the procedure employed were as follows: (1) carcinoma of the supra-ampullary portion, posterior gastro-enterostomy; (2) carcinoma of the periampullary portion, biopsy, posterior gastro-enterostomy and cholecystogastrostomy; (3) carcinoma of the infra-ampullary portion, gastro-enterostomy; (4) carcinoma of the periampullary portion, cholecystostomy, duodenotomy and biopsy, and carcinoma of the periampullary portion, cholecystogastrostomy and gastro-enterostomy.

There were 7 postoperative deaths (58.3 per cent). The location of the lesion and the operative procedures employed were as follows: (1) carcinoma of the supra-ampullary portion, posterior gastro-enterostomy; (2) carcinoma of the infra-ampullary portion, insertion of gold radon seeds; (3) carcinoma of the periampullary portion, duodenotomy and biopsy; (4) carcinoma of the infra-ampullary portion, anterior gastro-enterostomy; (5) carcinoma of the periampullary portion, cholecystostomy, duodenotomy and biopsy; (6) carcinoma of the periampullary portion, second stage duodenotomy and excision of the growth, and (7) carcinoma of the infra-ampullary portion, jejunostomy.

In 4 instances the duodenum was opened. Specimens for biopsy were taken in 3 instances, and in the fourth case the tumor was excised. Three of these patients died. The causes of death were, respectively, peritonitis, bronchopneumonia and shock.

Of the 5 patients who survived operation, 2 were not traced. One lived fourteen weeks and died at home. The 2 remaining patients (in whom the growth was not removed) lived two years.

SUMMARY

This paper presents a clinical and roentgenographic study of 18 cases of primary carcinoma of the duodenum collected from the material of the Memorial Hospital for the Treatment of Cancer and Allied Diseases, the New York Polyclinic Medical School and Hospital, the New York Post-Graduate Medical School and Hospital, the Lenox Hill Hospital and St. John's Long Island City Hospital, all of New York; the Paterson General Hospital, Paterson, N. J., and the New Haven Hospital, New Haven, Conn. In 5 of the cases the patient was studied during life by us. All were instances of true carcinoma of the duodenal mucosa. Cases of carcinoma of the ampulla or of the papilla of Vater are not included.

The rarity of primary carcinoma is indicated by its incidence of 0.033 per cent of 350,286 autopsies. The sex incidence shows a preponderance of males of 3:1.

The usual pathologic type is some form of adenocarcinoma arising from the duodenal mucosa. The gross forms may be scirrhus, bulky and polypoid, or colloid. The pathologic findings in these 18 cases are summarized in table 1.

The symptoms of duodenal carcinoma are chiefly those due to obstruction of the duodenum and neighboring structures. The early stages are featured by anorexia, gaseous eructations, epigastric distention and nausea. As obstruction develops, these become more severe, and pain, vomiting, dehydration, loss of weight and constipation quickly follow. A palpable tumor is found in more than half the cases. The sloughing away of portions of the tumor may temporarily relieve the obstruction or give rise to severe hemorrhage. When the bile passages are obstructed, jaundice of a constant, unremitting type develops. The progress of the disease is swift, and the loss of weight may be extreme.

The average duration of life is about seven months after the onset of symptoms. The shortest duration of life is found in cases in which the lesion is around the ampulla; the longest duration, in those in which the lesion is in the first portion of the duodenum.

In almost every case of duodenal carcinoma which is studied roentgenographically definite pathologic changes can be demonstrated. Such evidence was present on the films in 15 cases in which such studies were made. In 14 of these the pathologic process was recognized and described. In only 1 instance, however, was the possibility of a primary carcinoma of the duodenum suggested. The various roentgenographic findings are described at length and summarized in table 2.

The diagnosis and differential diagnosis are discussed in detail.

The treatment of primary carcinoma of the duodenum is preeminently surgical. The operative mortality is high. In a large percentage of cases at operation there is no evidence of metastasis or local extension of the disease. The surgical removal of all of the malignant tissue might therefore often be feasible if this mortality could be brought down to a reasonable level by efforts to combat the effects of the intestinal and biliary obstructions prior to operation. The patients show advanced degrees of starvation, dehydration, alkalosis, anemia, jaundice and gastric distention. Measures recommended in the preparation of the patient for operation are the restoration of body fluids, mineral salts, carbohydrates and blood supply. Various surgical procedures which have been employed are described, discussed and illustrated. The operative results obtained in the various procedures employed in 12 of this series of 18 cases are described and summarized.

REPORT OF CASES

CASE 1.—M. B., a woman aged 48, was admitted to the Memorial Hospital complaining of epigastric pain radiating to the back. The pain was of four months' duration and was severe and cramplike. It was intensified or precipitated by the taking of food, but was not relieved by alkalis and was not accompanied by vomiting. The patient's appetite was good, but she feared to eat because of the pain thus initiated. Loss in weight was moderate but progressive. Physical examination revealed an emaciated woman of 48. The abdomen was sunken, and a hard, smooth, movable mass 5 cm. in diameter could be palpated in the midline immediately above the umbilicus. The liver was not palpable. Roentgenographic and fluoroscopic examination of the gastro-intestinal tract revealed a constant widening of the pyloric sphincter and irregularity in the outline of its surfaces. The duodenal cap was small and slightly deformed but fairly well filled. Beyond the cap there was some irregularity in the outline and distribution of the barium sulfate in the lumen, but the remaining portions appeared normal (fig. 6). Peristalsis was active; there was little delay in the passage of the barium, and no gastric retention was present after six hours. The constant widening of the pylorus was interpreted as suggestive of an annular carcinoma or a fibrotic process as the result of an old pyloric ulcer. Gastric analysis showed normal amounts of free hydrochloric acid. A clinical diagnosis of carcinoma of the pylorus was made. At operation a tumor 5 by 4 by 4 cm. was found involving the posterior wall of the duodenum immediately distal to the pylorus. The tumor had invaded the pancreas, rendering its removal impossible. Posterior gastro-enterostomy was performed, and the abdomen was closed. Four days after operation bilateral parotitis developed, and the swellings became so great that they compressed the pharynx and caused extreme dysphagia and dyspnea. The respiratory difficulty was relieved by an emergency tracheotomy, but death occurred two hours later.

At autopsy a hard ulcerated mass 5 by 4 by 4 cm. was found in the first portion of the duodenum 2 cm. below the pylorus. Metastatic masses were found in the mesenteric nodes of the duodenum, transverse colon and rectum. The liver was not involved. Microscopic examination of the duodenal tumor revealed a malignant adenoma.

CASE 2.—D. H., a woman aged 28, had attacks of severe epigastric pain in August 1929. These were accompanied by nausea and vomiting; during the next two months there was marked loss of weight and strength. Her physician discovered an oval mass in the upper part of the abdomen slightly to the left of the midline. An exploratory laparotomy at the Brownsville and East New York Hospital in December 1929 disclosed a mass the size of an orange at the duodeno-jejunal angle, apparently retroperitoneal in location. No specimen was taken for biopsy. A clinical diagnosis of retroperitoneal lymphosarcoma was made. Immediately after convalescence the patient received twelve treatments by high voltage roentgen therapy. This was followed by the complete disappearance of the abdominal tumor; she gained 20 pounds (9 Kg.) and was restored to her former strength. All symptoms disappeared temporarily, but six months later the tumor recurred and soon reached the size of a grapefruit. Recourse again was had to roentgen therapy, but the tumor did not respond. Symptoms increased in severity, and the patient was referred to the Memorial Hospital. Roentgenograms of the gastro-intestinal tract showed no deformity of the duodenal cap or retention of barium after six hours. The curving loop made by the course of the duodenum, however, was greatly widened as though the expansive growth of a tumor in that location had thrust the duodenum aside (fig. 7). A diagnosis of retroperitoneal sarcoma

or carcinoma of the head of the pancreas was made, and an exploratory laparotomy was performed by Dr. Frank E. Adair. A rounded, globular tumor mass containing several cystic areas was found apparently retroperitoneally beneath the duodenum and the jejunum. It was impossible to remove the mass, and an attempt was therefore made to accomplish its destruction with interstitial radiation. Twenty-two gold radon seeds containing 55.51 millicuries of radon were inserted into the mass and spaced 1 cm. apart. The patient's condition postoperatively was poor, and death occurred four days later. At autopsy a mass of cancerous tissue was found completely surrounding the duodenum and causing partial constriction. The tumor tissue was white, opaque and partly necrotic as a result of the irradiation. Its texture suggested lymphosarcoma. The mesenteric nodes and the liver were not involved. The stomach was greatly dilated. Microscopic study showed a primary anaplastic adenocarcinoma of the duodenum (fig. 8).

CASE 3.—B. K., a woman aged 60, presented a history of "stomach trouble" for the past five years. Four months before she came to the Memorial Hospital there developed pain in the right upper quadrant, anorexia, loss of weight and moderate constipation. Roentgenograms made elsewhere and not available for study were said to have shown carcinoma of the hepatic flexure of the colon. At this time the patient noted marked feeling of distention after eating. Physical examination disclosed the following abnormal findings: emaciation, dehydration, anemia, edema of the extremities and a slightly movable, irregular, nontender mass the size of an orange in the region of the right kidney. Urologic studies showed diminished function of the right kidney, with many pus cells in the urine. A pyelogram showed changes interpreted as a destructive process in the right kidney, probably inflammatory in nature. A roentgenographic study of the gastrointestinal tract disclosed a filling defect in the prepyloric segment of the stomach and evidence of upward displacement of the duodenum, pressure on the greater curvature of the gastric antrum, with filling defects in the stomach and duodenum. Some evidence of infiltration of the pylorus and in the descending portion of the duodenum was noted. There was marked retention after six hours (fig. 9). These findings were interpreted as possibly being caused by a tumor of the head of the pancreas. Exploratory laparotomy revealed a large mass 6 by 4 cm. in diameter adherent to the posterior surface of the stomach, apparently arising from the duodenum and impossible to remove. The duodenum was opened, a biopsy specimen was removed, and the duodenum was closed with silk sutures. The abdomen was closed; on the sixth postoperative day bronchopneumonia developed, and the patient died five days later.

Autopsy disclosed focal and pelvic peritonitis as the results of a breakdown of the suture line in the duodenum, a fecal fistula and bronchopneumonia. Surrounding the ampulla of Vater and extending for 6 cm. along the lumen and partly obstructing it, was an annular, polypoid primary carcinoma of the duodenum. There was no evidence of metastases. Microscopic study showed primary malignant adenoma of the duodenum (fig. 11).

CASE 4.—C. S., a woman aged 47, was admitted to the Memorial Hospital on Feb. 17, 1931, with the complaint of weakness, loss of weight, fatigue, nausea and vomiting. These symptoms had arisen four months before and had steadily become more marked. The vomiting appeared to have no relation to meals, and the vomitus usually contained bile. There had been no jaundice until a few weeks prior to admission, when a transitory attack occurred, accompanied by fever. During the past twelve years there had been many attacks of pyuria. Examination disclosed a middle-aged woman in fair general condition. In the right

upper quadrant of the abdomen a mass was palpable which appeared to be an enlarged right kidney. A pyelogram showed hydronephrosis of the right kidney. On February 28 the right kidney was removed by Dr. Benjamin Barringer. The specimen contained a broken-down hypernephroma measuring 8 by 7 by 5 cm., the bulk of which showed gross caseous necrosis. The renal pelvis was dilated at the lower pole, where there was marked hydronephrosis. The microscopic diagnosis was "papillary adenocarcinoma of the renal tubule type, with clear and granular cells." The patient made a smooth recovery and felt moderately better for about six weeks, after which there was a return of weakness, nausea and vomiting. She lost weight rapidly, and in June 1931, four months after operation, increasing jaundice, anemia and fever developed. Vomiting of bile-stained fluid became more frequent. She received a transfusion of blood, and for a time improved in general health. Late in July her temperature rose daily to 104 F., accompanied by chills and a steadily increasing jaundice. The stools became clay colored and offensive. Vomiting occurred several times a day, and the vomitus often contained clots of blood as well as coffee-ground material. When readmitted to the Memorial Hospital at this time she was profoundly ill and deeply jaundiced and had lost a great deal of weight. She complained of a dull pain in the epigastrium, which was relieved only by vomiting. The urine was highly colored with bile and hemoglobin. The temperature during the chills rose to 105 F. and occasionally to 106 F. The patient was greatly dehydrated and appeared to be moribund. Large amounts of fluids and dextrose were administered intravenously. The blood count on admission showed 1,550,000 red cells, 14,400 white cells and a hemoglobin content of 40 per cent. The differential count showed 91 per cent polymorphonuclear leukocytes. Three transfusions of a total of 1,950 cc. of whole blood were given within forty-eight hours after admission. The stomach was greatly dilated, and large quantities of blood-stained fluid were removed by gastric lavage. This fluid contained identifiable patches of desquamated gastric mucosa. An attempt at duodenal drainage failed to demonstrate evidence of the patency of the common bile duct. The patient's condition was extremely poor. Vomiting of bright red blood occurred on two occasions, after which the patient grew rapidly weaker and died. No definite diagnosis was made prior to death, although the general picture appeared to indicate a high degree of biliary obstruction and infection. The most likely cause for this was thought to have been a recurrence of the hypernephroma of the right kidney. Roentgenograms made several weeks prior to the last admission showed hypomotility, a large duodenal cap and an irregular outline of the second portion, indicating partial duodenal obstruction.

Autopsy revealed an extreme degree of jaundice; the liver was normal in size, dark green and markedly congested. The gallbladder, common bile duct and hepatic ducts were greatly dilated. One could readily pass a finger down the common bile duct to the ampulla of Vater, which was obstructed by a mass within the duodenum. The stomach was distended to three times its normal size, and the pylorus was widely dilated (fig. 14). The first portion of the duodenum was similarly widely distended. Ten centimeters from the pylorus there was a large, papillary, ulcerated growth involving the entire circumference of the duodenum and extending along the lumen for a distance of 6 cm. This tumor surrounded the ampulla of Vater and completely obstructed it, so that the common duct and the remainder of the biliary system were greatly dilated. There was no evidence of any metastases anywhere in the body and no evidence of any recurrence of the previous hypernephroma of the right kidney. Microscopic study of the tumor of the duodenum showed a primary malignant adenoma (fig. 9). Com-

parison of the duodenal tumor with the mass previously removed with the right kidney (fig. 12) showed them to be two histologically distinct tumors, and it was the opinion of Drs. Ewing and Stewart that this was a proved example of multiple primary malignant growth.

CASE 5.—H. S., a white German woman aged 68, was admitted to the Lenox Hill Hospital on Nov. 4, 1932, complaining of pain in the epigastrium, vomiting, loss of 20 pounds (9 Kg.) in weight and increasing weakness. Symptoms were of three months' duration. On one occasion eight months prior to admission and five months before the onset of symptoms she noted bright red blood in the stools. Examination showed a thin, pale elderly woman, who had evidently lost considerable weight. The edge of the liver was barely palpable. There was a slightly palpable tender mass in the midepigastrium. The stomach was dilated, and an audible splash could be demonstrated. A roentgenographic study of the gastro-intestinal tract disclosed a persistent filling defect in the duodenum at the junction of the first and the second portion. The duodenal wall was markedly rigid, and the filling defect was persistent and caused considerable obstruction, so that at the forty-eighth hour considerable barium was retained within the stomach. The report made by Drs. William H. Stewart and H. E. Illick suggested the possibility of malignant obstruction of the duodenum. On November 9 the abdomen was explored by Dr. Herman Fischer, who found the stomach to be greatly dilated and its walls markedly hypertrophied. The pyloric ring was normal. Beginning on the distal side of the ring and involving the first and second portions of the duodenum was a hard, elastic, whitish tumor tissue which Dr. Fischer considered unquestionably malignant and not inflammatory. There was no evidence of metastases or local extension. A posterior gastro-enterostomy was performed. No biopsy was made. The postoperative course was smooth, and the patient left the hospital in relatively good condition. Two years later reexamination showed the gastro-enterostomy stoma functioning well. There was a constant rounded shadow present which deformed the duodenum and prepyloric area of the stomach. This was considered to be the greatly increased size of the mass found at operation.

CASE 6.—L. H., a 70 year old German woman, was admitted to the Lenox Hill Hospital to the service of Dr. Carl Theobald in December 1930, complaining of persistent vomiting and a viselike pain around the upper portion of the abdomen and epigastrium of five weeks' duration. This pain usually subsided after the stomach had been emptied by vomiting. The patient had never been jaundiced. Examination revealed an elderly, emaciated woman in poor physical condition. The stomach was greatly distended, as indicated by marked tympany over most of the abdomen. The diagnosis on admission was obstruction of the pylorus of unknown etiology. After the administration of large amounts of fluids and stimulants, the stomach was emptied by lavage. A roentgenographic study of the gastro-intestinal tract revealed a high grade pyloric obstruction, so that at the sixth hour only 10 per cent of the barium had passed out of the stomach. The character of the obstruction could not be determined from the roentgenograms, although a malignant growth and ulcer were suggested as the most likely causes. Three days later the patient suddenly became weaker and cyanosed, the temperature remained elevated, the pulse grew feeble and she died, apparently of a terminal myocardial failure.

At autopsy the gallbladder was found adherent to the duodenum and communicating with it through a spontaneous cholecystoduodenostomy opening. The stomach was greatly dilated, with thickening of the wall in the pyloric region. The first portion of the duodenum immediately distal to the pylorus was obstructed

by an ulcer with a raised necrotic border and base. The surrounding area was indurated and infiltrated. There were no evidences of metastases. The lumen of the small intestine was filled with a large amount of red blood.

Microscopic examination of the ulcerated tumor of the duodenum disclosed adenocarcinoma containing a few areas of anaplastic squamous carcinoma. This case was briefly referred to by Sauer³⁵ in a discussion of the possibility of carcinoma of the duodenum arising on the basis of a previous duodenal ulcer.

CASE 7.—M. B., a French woman aged 51, was admitted to the Lenox Hill Hospital on Aug. 28, 1930, complaining of loss of weight, weakness, nausea and vomiting of three months' duration. At the time of admission she had lost 40 pounds (18 Kg.) in weight, and the attacks of vomiting occurred several times a day precipitated by the taking of any food or drink. Examination disclosed an obese white woman whose skin was a muddy yellow. She was drowsy, weak and dehydrated because of severe vomiting. Study of the blood chemistry revealed a marked increase in all constituents, probably due to dehydration. The carbon dioxide-combining power was 73.9. Examination of the gastro-intestinal tract revealed no changes recognizable as cancer or ulcer. There was no roentgenographic indication of obstruction anywhere. The patient's condition became steadily worse despite all efforts, and she died six days after admission.

At autopsy the stomach was greatly dilated with gas. In the left upper quadrant of the abdomen was a tumor involving the distal portion of the duodenum and the proximal portion of the jejunum, which was bound down tightly to the splenic flexure and to the transverse colon. The lumen of the duodenum was almost completely occluded by a polypoid tumor, which was extensively ulcerated. This tumor was soft and invaded the duodenal wall in many areas and formed nodules on its outer surface. It encircled the entire duodenum and measured 11 cm. on its long axis. There was no involvement of the liver, nodes or any other structures.

Microscopic study of the tumor showed a small cell adenocarcinoma with extensive areas of spontaneous necrosis.

CASE 8.—C. A., a housewife aged 52, entered the New York Polyclinic Medical School and Hospital on Feb. 18, 1932, complaining of jaundice and pain in the epigastrium. Six weeks previously she noted that her skin and conjunctivae were yellow. Three days later she experienced pain in the right upper quadrant, which she described as "feeling like a dead weight." Soon afterward she had attacks of nausea and vomiting. For the past three months she had a distaste for fats and lost weight and strength. The stools were bloody; constipation steadily increased. The patient was treated by administration of fluids and dextrose and other supportive measures but died one week after admission. Because of her moribund condition no roentgen studies were made of the gastro-intestinal tract except for films of the gallbladder, which were unsatisfactory for diagnosis. Because of respiratory movements.

Autopsy, performed by Dr. Aaron S. Price, disclosed a jaundiced, emaciated woman. The stomach was enormously dilated. The gallbladder was dilated to a diameter of 8 cm. Arising in the periaampullary portion of the duodenum was a carcinoma which had obstructed the ampulla and had secondarily invaded the pancreas. Microscopic study of the tumor showed malignant adenoma and adenocarcinoma, partly diffuse, arising from mucous glands with tendencies toward squamous metaplasia (fig. 18).

35. Sauer, P. K.: Carcinoma Following Gastric and Duodenal Ulcer, *Ann. Surg.* **102**:295, 1935.

CASE 9.—H. B., a man 78 years old, was admitted to the New York Polyclinic Medical School and Hospital on Feb. 23, 1931, complaining of pain in the epigastrium, loss of weight, nausea and vomiting after taking food. The vomitus was greenish and copious, and vomiting was followed by marked symptomatic relief. These symptoms were of six weeks' duration, during which time he had lost 25 pounds (11 Kg.) in weight. Constipation was of long standing. Physical examination disclosed an elderly man, chronically ill, disoriented, dehydrated and feeble. An irregular mass was palpable in the epigastrium. The stomach was greatly dilated and was boldly outlined through the abdominal wall. The intern made a note that despite negative roentgenograms said to have been made elsewhere prior to admission, he believed that the patient had an obstruction somewhere in the duodenum, either from a new growth or from adhesions. A serial roentgenographic study of the gastro-intestinal tract showed "gastric retention due to obstruction of the duodenum, probably caused by adhesions of the second and fourth portions. Involvement of the pancreas should be suspected. The changes found may be due to pancreatitis, ulcer of the duodenum, or tuberculous infection of the peritoneum." The patient was in extremely poor condition. After great efforts to get him in condition for operation by administration of dextrose and fluids by all routes, a laparotomy was done by Dr. Robert E. Brennan with the patient under spinal anesthesia, and an anterior gastro-enterostomy with entero-enterostomy was performed. The patient died several days later.

Autopsy, performed by Dr. Aaron S. Price, disclosed diffuse peritonitis apparently arising from the region of the gastro-enterostomy. The intestine was semi-gangrenous, with no attempt at healing. In the terminal portion of the duodenum, just above the duodenojejunal junction, was a hard white tumor which had ulcerated and encircled the lumen to produce almost total obstruction. The proximal portion of the duodenum and the stomach were dilated. There was no evidence of local extension or metastases. Microscopic study showed adenocarcinoma arising from cells of the glands of Lieberkühn.

CASE 10.—A. B., a man aged 71, entered the Paterson General Hospital complaining of dizzy spells, sudden transitory attacks of unconsciousness, a feeling of constriction in the esophagus and frequent attacks of dyspepsia with gaseous eructations. There was no history of vomiting or of gross blood in the stools. During the past several months there had been some progressive enlargement of the abdomen. Examination revealed a large indirect inguinal hernia and a hydrocele on the right side and moderate abdominal ascites. No operation was performed except paracentesis. Examination of the stools showed the presence of blood. Roentgenographic studies of the gastro-intestinal tract made after the administration of barium showed that the stomach was not dilated and that peristalsis was active. The first portion of the duodenum was obscured by the antrum of the stomach. The second portion was irregularly deformed and narrowed. No definite diagnosis was made. Permission for exploratory laparotomy was refused. Three months later the patient died.

Autopsy disclosed a broad, annular, papillary and infiltrating carcinoma, 8 cm. in diameter, completely encircling the lumen of the duodenum, arising at a point 1 cm. below the papilla of Vater. The mass was ulcerated and firm and had a border 3 cm. in thickness. There were miliary metastases to the visceral and parietal peritoneum, liver and lymph nodes. Microscopic study showed adenocarcinoma of the duodenum, grade 2. (Dr. William Wuester and Dr. A. Hobson Davis of the Paterson General Hospital permitted us to report this case.)

CASE 11.—S. A., an Italian youth 18 years of age, was admitted to the New York Post-Graduate Medical School and Hospital on March 2, 1915, complaining of pain in the epigastrium, loss of weight and a mass in the epigastrium. The first symptom of epigastric pain developed one year prior to admission and was consistently aggravated by eating. Physical examination revealed a fairly well nourished, anemic youth. There was no jaundice. In the epigastrium, slightly to the right of the midline, a hard mass about 5 cm. in diameter could be palpated. The mass was slightly movable, particularly with respiration. The liver was not enlarged, although an enlarged gallbladder could be palpated close to the hard mass already described. Four weeks after admission the skin and conjunctivae showed jaundice, which within two weeks increased markedly. The stools became pale and the urine was dark with bile. A roentgenogram of the region of the gallbladder showed a shadow of an enlarged viscus but no stone. A serial roentgenographic study of the gastro-intestinal tract showed irregularity of the second portion of the duodenum, which curved far out to the right. In the middle of the first portion of the duodenum there was noted a persistent fleck of bismuth, which was still present six hours later. At this time there was a small gastric residue. The findings were interpreted as a perforating ulcer of the inferior horizontal portion of the duodenum. On March 23 the abdomen was explored by Dr. John Erdmann, who found a tumor, 8 cm. in diameter, in the second part of the duodenum, surrounding the ampulla of Vater. A large piece of the tumor was excised for biopsy, and posterior gastro-enterostomy and cholecystogastrostomy were performed. There was no evidence of extension or metastases at operation. The postoperative course was smooth, and the patient was discharged from the hospital much improved three weeks later. He never returned for examination and remained untraced. Pathologic examination of the biopsy specimen showed a smooth, lobulated mass, measuring 4 by 3 by 2 cm. Microscopic study showed a fairly aggressive adenocarcinoma growing in disorderly fashion in a fibrous stroma.

CASE 12.—E. D., a woman aged 56, was admitted to St. John's Long Island City Hospital on March 6, 1935, under the care of Dr. Emanuel F. Kalina, complaining of loss of weight, appetite and strength and of chills, fever and jaundice. Two months prior to her illness she began to have pains in the limbs and fever, chills and profuse perspiration. The temperature ranged from 102 to 104 F. The stools became pale, soft or watery, and the skin and conjunctivae became jaundiced. The ingestion of food brought on sour eructations, distention of the epigastrium, nausea and belching of gas, but no vomiting. Examination disclosed jaundice, loss of weight, tenderness in the epigastrium and muscular spasm over the area of the gallbladder. The liver and gallbladder were not palpable. The red cell count was 3,080,000, the white cell count 26,300 and the hemoglobin content, 51 per cent. The icteric index was 35. The van den Bergh direct reaction was positive in thirty seconds. Occult blood was present in the stools. Roentgenograms of the gastro-intestinal tract made after a barium meal showed a normal stomach. The duodenal cap was greatly enlarged, triangular in shape and regular in outline. The descending portion was irregular and narrowed, and barium was retained in the second portion for more than twenty-four hours (figs. 21, 22 and 23). These findings were interpreted as indicating a duodenal diverticulum with partial obstruction. In view of the symptoms of jaundice and fever, indicating biliary obstruction, and the appearance of the duodenum in the films, a diagnosis of possible carcinoma of the head of the pancreas was considered, and exploratory laparotomy was advised. At operation by Dr. William J. Lavelle a markedly distended gallbladder was found. A mass was palpated in the second

portion of the duodenum. This was exposed through a small incision and found to be a polypoid carcinoma surrounding the region of the ampulla. The proximal portion of the duodenum was greatly dilated. The duodenal obstruction was partly relieved by freeing adhesive bands in the region of the growth. A portion was excised for biopsy, and the duodenum was closed in two layers. A rubber drainage tube was inserted into the gallbladder and brought out through the incision. Post-operatively, there was profuse drainage of bile from the tube and from a Levine tube introduced into the stomach through the mouth. On the third postoperative day, bronchopneumonia developed, and the patient died four days later.

Autopsy disclosed a friable, polypoid tumor surrounding the region of the papilla but arising in the duodenum (fig. 24). The gallbladder and common duct were dilated. The liver was smooth and green. There was no evidence of local extensions or metastases. The suture line around the opening in the duodenum was intact. Microscopic study of the specimen showed a papillary adenocarcinoma of the duodenum (fig. 25).

CASE 13.—J. R., a man aged 51, complained of sour stomach and heartburn of two years' duration, with nausea, vomiting and epigastric pain of eight weeks' duration. Six weeks prior to admission a roentgenographic study of the gastro-intestinal tract revealed retention of barium after six hours. He had lost 30 pounds (13.6 Kg.) in the past six weeks, his weight falling from 171 to 141 pounds (77.6 to 64 Kg.). Physical examination showed a markedly emaciated patient. Urinalysis showed the presence of sugar. Roentgenograms of the gastro-intestinal tract revealed obstruction of the third portion of the duodenum with marked dilatation of the entire duodenum and retention of barium within the stomach and duodenum after six hours (fig. 26). A diagnosis of duodenal obstruction was made. The operation was performed by Dr. John F. Erdmann, on May 25, 1929, and a carcinoma of the terminal portion of the duodenum was found. There were multiple metastases found in the liver. A gastro-enterostomy was done, and the patient was discharged from the hospital nineteen days later. He subsequently was untraced.

CASE 14.—W. F., a man aged 45, complained of nausea, vomiting, epigastric pain and distention. Previous examination at another hospital had not yielded a definite diagnosis, and an exploratory laparotomy had been advised. A roentgenographic series of the gastro-intestinal tract showed the terminal portion of the duodenum distinctly outlined by the barium in a manner which suggested some obstruction of the lumen, but this escaped detection at the time and was noted only after the patient had been operated on. Dr. Erdmann's clinical diagnosis was carcinoma of the liver with generalized abdominal carcinomatosis. At operation on Sept. 21, 1927, a definite carcinoma of the terminal portion of the duodenum was found. There was an extensive generalized carcinomatosis involving all the abdominal structures in addition to bulky metastases in the liver. A palliative jejunostomy was performed. The patient failed steadily and died twelve days after operation. Permission for autopsy was not obtained.

CASE 15.—F. K., a woman aged 36, was admitted to the New Haven Hospital on April 24, 1935, complaining of weakness, anorexia and a constant dull pain in the right upper quadrant which had been present for two months. A month prior to admission she had an attack of severe pain in the same region, associated with a progressively increasing jaundice. The pain radiated through to the back. The skin became yellow, the stools were pale and clay colored, and the patient lost weight steadily. There was no nausea, vomiting or tarry stools. Physical examination showed marked jaundice, tenderness in the region of the gallbladder, rigidity of

the abdominal muscles and enlargement of the liver. The red cell count was 4,200,000, the white cell count 13,600 and the icteric index 100. The van den Bergh test was positive. The stools were negative for occult blood or bile. A diagnosis of chronic cholecystitis and cholelithiasis was made, and on May 5 an exploratory laparotomy revealed a large, tense gallbladder and a mass in the region of the ampulla, which was thought to be an impacted stone. Because of brisk bleeding which occurred, the only procedure attempted was the insertion of a drain into the gallbladder. Twenty-six days later the abdomen was again explored in the service of Dr. S. C. Harvey, and a large friable, cauliflower mass was found surrounding the ampulla of Vater. The duodenum was opened and a biopsy specimen was removed. The postoperative course was stormy, and a fecal fistula developed in the lower angle of the wound. The patient left the hospital in poor condition, became progressively worse and was brought back to the hospital, where she died on September 9.

Autopsy disclosed a markedly emaciated woman weighing only 65 pounds (29 Kg.). There was a fecal fistula leading down to the transverse colon. The stomach was markedly distended to five times normal size and filled nearly the entire abdominal cavity. The proximal duodenum was distended to four times its normal size. The ampulla of Vater was surrounded by a friable, fungating tumor mass 3 cm. in diameter, which occluded the lumen. The lymph nodes of the celiac and peripancreatic regions were enlarged and obviously involved by metastases. The liver was not involved, although the pancreas was directly invaded. Microscopic examination of a specimen from the periampullary tumor showed an adenocarcinoma of high columnar cells.

CASE 16.—A. B., a man aged 58, was admitted to the Lenox Hill Hospital, service of Dr. Robert C. Schleussner, with a complaint of attacks of fever lasting only one or two days, accompanied by chills, intermittent jaundice and tenderness in the right upper quadrant. Roentgenograms of the abdomen made without the administration of any dye showed the gallbladder clearly outlined and enlarged. This appearance was interpreted as evidence of chronic cholecystitis. Roentgenograms and fluoroscopy of the gastro-intestinal tract made after the administration of barium revealed no evidence of ulcer or cancer in the stomach or duodenum. The second portion of the duodenum, however, showed some deformity, which was considered to be due to adhesions. There was no gastric residue at six hours. Physical examination disclosed the following positive findings: moderate jaundice, fever and tenderness in the right upper quadrant. The stools did not contain bile; the urine was colored with bile. After a clinical diagnosis of impacted stone in the common duct, exploratory operation was done by Dr. Otto C. Pickhardt, and the common duct found to be obstructed at the ampulla. The dilated duct was explored, but no stone found. Because of the patient's condition it was thought inadvisable to search further for the cause of the obstruction at this stage, and the operation was terminated with the insertion of a T tube into the duct to relieve the biliary obstruction. Postoperatively there was a profuse drainage of bile from the tube, and the jaundice cleared up within a week. The condition of the patient improved slowly. Four weeks after the operation he suddenly vomited a large quantity of bright red blood and simultaneously began to bleed from the abdominal wound. A transfusion of 400 cc. of whole blood was immediately given to the patient. On the following day the wound was opened and large blood clots removed. No source of the bleeding was found. The duodenum was exposed, and a small mass was palpable in the second portion. The duodenum was opened, and a soft, friable tumor mass was found on the posterior

surface close to the ampulla. This was excised, and the duodenum was closed. There was no evidence of metastases within the abdomen. Six hours later the patient died. Microscopic examination of the specimen removed from the duodenum showed adenocarcinoma.

CASE 17.—G. B., a woman aged 45, complained of epigastric pain, nausea and vomiting. Symptoms had been present for six weeks. A roentgenographic study of the gastro-intestinal tract showed obstruction of the second portion of the duodenum. Operation by Dr. John F. Erdmann disclosed a large tumor mass which had almost completely encircled and obstructed the periampullary portion of the duodenum. The obstruction was relieved by cholecystogastrostomy and posterior gastro-enterostomy. The postoperative course was smooth, and the patient lived for two years and died at home. Permission for autopsy was not obtained.

CASE 18.—C. G., a woman aged 45, entered the Lenox Hill Hospital on Feb. 13, 1936, service of Dr. Abraham L. Garbat, complaining of intermittent fever, jaundice, pain in the right upper quadrant, pruritis, loss of weight, weakness, anorexia and vomiting. The symptoms began one year prior to admission and had persisted thereafter, except for four short remissions during that time. Roentgenograms of the gastro-intestinal tract made twelve months before admission showed no definite abnormality of the stomach or duodenum. Physical examination revealed a markedly jaundiced woman in an extremely poor condition because of sepsis, vomiting and dehydration as the consequence of biliary and duodenal obstruction. The urine was dark and contained considerable bile. The stools were clay colored and were negative for tests for bile. The icteric index was 133; the carbon dioxide-combining power was 34 volumes per cent. Analysis of the duodenal contents on seven occasions showed only slight evidence of bile. After the intravenous administration of dextrose in saline solution the patient's condition improved slightly, but two days after admission she suddenly became restless, passed into shock and died.

Autopsy disclosed a markedly jaundiced, emaciated woman about 45 years of age. When the abdomen was opened a massive hemorrhage was found behind the peritoneum, within the peritoneal cavity and inside the lumen of the small intestine. Both pleural cavities contained considerable clear fluid. The liver was dark green and enlarged and extended 5 cm. below the costal margin. The gall-bladder had been removed at operation eleven years before. The bile and pancreatic ducts were greatly dilated, the common duct measuring 1.5 cm. in diameter. Surrounding the ampulla of Vater was a raised, polypoid ulcerated tumor, 2.5 cm. in diameter. There was no evidence of metastasis or extension anywhere within the abdomen. Microscopic examination of the duodenal tumor showed adenocarcinoma.

ABSTRACT OF DISCUSSION

DR. E. V. POWELL, Temple, Texas: The paper by Drs. Hoffman and Pack recalls a case that I reported to the New York Roentgen Society while I was at St. Bartholomew's Hospital. It was one of duodenal carcinoma, which I was lucky enough to diagnose as a tumor. It was an adenocarcinoma and gave a filling defect about the size of a golf-ball within the duodenal cap. Obstruction was almost, but not entirely, complete. I have since seen one other carcinoma of the duodenum which arose near the papilla and terminated fatally. In the first case operation was performed and radon seeds were implanted. The patient lived long enough to get away from the hospital, but I do not know what happened to him later.

DR. ROSS GOLDEN, New York: Drs. Hoffman and Pack's unfortunate experience with roentgen diagnosis of carcinoma of the duodenum should be a stimulus to roentgenologists. Carcinoma of the duodenum can be correctly interpreted by roentgen examination.

One of the young men of the hospital, who had only about three or four years' experience in roentgenology, correctly made such an interpretation a few years ago, based on the fact that the mucous membrane of the second portion of the duodenum was destroyed over one side. The mucosal folds of the duodenum below the first portion are marked, making that kind of an interpretation relatively easy.

One must become acutely conscious of the mucous membrane of the gastrointestinal tract. Within a year one of the residents at the hospital with which I am associated demonstrated a duodenum in which the mucous membrane was destroyed from about the beginning of the second portion clear through the second portion into the jejunum. He thought it was probably not a carcinoma and raised the question of a lymphoblastoma. The pathologist called the growth a lymphosarcoma, and the patient has improved under roentgen treatment.

CARE OF THE SEVERELY BURNED

WITH SPECIAL REFERENCE TO SKIN GRAFTING

EARL C. PADGETT, M.D.

KANSAS CITY, MO.

From my experience with the care of the severely burned, I believe that the following points are especially important: 1. During the first day or so the systemic changes assume a position of greater importance than the local injury. 2. Later in the care of the local lesion the use of fundamental principles of cleanliness and good drainage, in contradistinction to the use of this and that preparation or technic which ignores these principles, represents sound treatment. 3. Insistence on the necessity of early resurfacing of the resultant granulating surface should be stressed because of the marked decrease in the period of convalescence with its economic potentialities and the extent to which functional incapacitation from contracture or cosmetic blemishes can be forfended. 4. When the time for skin grafting is at hand, dependence on fundamental principles and methods, in contradistinction to the use of unusual types of grafts with or without a "far-fetched" method of placement, puncturing or dressing, usually will tend toward real success.

In a series of 514 skin grafts which were transplanted at 361 separate operations on 257 different persons, 299 of the grafts were transplanted at 193 separate operations on 144 different persons to alleviate the damage resulting from a burn of one type or another. Moreover, for my purpose the damage found either of a potentially deforming or of an actual contractural character in a series of burned persons presents most of the situations necessary to exemplify the principles involved in the successful grafting of skin.

EARLY CARE

In the group of 144 burned persons for whom skin grafting to a granulating surface was eventually necessary, 32 were cared for at one stage or another of a large severe acute burn. Not included in this

From the Department of Surgery of the University of Kansas School of Medicine.

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group are 5 persons, 3 of whom died within from one to three days after the burn and 2 of whom died of complications in the intermediate period before skin grafting could be completed.

Systemic Treatment.—Most of the emphasis in these cases was focused early on the alleviation of the profound systemic disturbance which occurred when the burn was of extensive proportions. In the patients seen immediately after being burned systemic treatment was based on the premise that besides considering an adequate amount of morphine for the alleviation of pain as a *sine qua non* and attempting to preserve normal body temperature, the salient point in the treatment was the early and more or less continuous replacement by substitution of that which had been lost and was being lost from the "circulatory tree." The work of Underhill and his co-workers¹ and Blalock² on the severely burned has served to draw attention to the rapid loss of blood plasma from the circulatory tree in amounts which soon may cause death. The lost plasma apparently tends to accumulate in the tissues adjacent to the area burned, and the mechanism of reabsorption tends to be rather negligible during the first thirty-six to forty-eight hours.

Main reliance for the purpose of dilution and replenishment of the fluids was placed on hypotonic saline solution. To replenish the protein lost from the circulatory fluids, autogenous blood was considered the solution nearest to that of the normal fluid. As a rough index

1. Underhill, F. P.; Carrington, G. L.; Kapsinow, R., and Pack, G. T.: Blood Concentration Changes in Extensive Superficial Burns and Their Significant Systemic Treatment, *Arch. Int. Med.* **32**:31-49 (July) 1923. Underhill, F. P.: The Lethal War Gases, New Haven, Conn., Yale University Press, 1920: The Physiology of Experimental Treatment of Poisoning with the Lethal War Gases, *Arch. Int. Med.* **23**:753-770 (June) 1919. Underhill, F. P.; Kapsinow, R., and Fisk, M. E.: Studies on the Mechanism of Water Exchange in the Animal Organism: I. The Nature and Effects of Superficial Burns, *Am. J. Physiol.* **95**:302-314, 1930; II. Changes in Capillary Permeability Induced by a Superficial Burn, *ibid.* **95**:315-324, 1930. Underhill, F. P.; Fisk, M. E., and Kapsinow, R.: III. The Extent of Edema Fluid Formation Induced by a Superficial Burn, *ibid.* **95**:325-329, 1930. Underhill, F. P., and Fisk, M. E.: IV. The Composition of Edema Fluid Resulting from a Superficial Burn, *ibid.* **95**:330-333, 1930. Underhill, F. P.; Fisk, M. E., and Kapsinow, R.: V. The Relationship of the Blood Chlorides to the Chlorides of Edema Fluid Produced by a Superficial Burn, *ibid.* **95**:334-338, 1930; VI. The Composition of Tissues Under the Influence of a Superficial Burn, *ibid.* **95**:339-348, 1930. Underhill, F. P., and Fisk, M. E.: VII. An Investigation of Dehydration Produced by Various Means, *ibid.* **95**:348-363, 1930; VIII. A Study of Dehydration by Pilocarpine Under Varied Dietary Conditions, *ibid.* **95**:364-370, 1930.

2. Blalock, Alfred: Experimental Shock: VII. The Importance of the Local Loss of Fluid in the Production of Low Blood Pressure After Burns, *Arch. Surg.* **22**:610-619 (April) 1931.

to the amount of solution needed, the extent³ and severity of the burn were considered in relationship to the size and age of the patient, and by means of periodic determinations of the blood pressure and repeated estimates of the hemoglobin content, the amount of plasma lost and the degree of blood concentration were roughly estimated. In a few instances adults received as much as from 4 to 8 liters of isotonic saline solution per day. The work of Smith and Mendel⁴ and of Rowntree⁵ on water intoxication indicates the safety of these amounts. Sometimes, if the patient was a child with some evidence of acidosis, a 5 per cent solution of dextrose in amounts to alleviate the symptoms was considered advisable. Repeated transfusions of blood were given according to the probable degree of the loss of plasma. When the oxygen-combining power of the blood was lowered, sodium bicarbonate was given in sufficient quantities to turn the urine alkaline. Ordinarily, after the first forty-eight hours, the systemic treatment simmered down to attention to a relatively high fluid intake and output and general symptomatic care of the patient. For preservation of a normal body temperature, an overhead canopy heated by electric lights was found to be efficient.

Early Local Care.—The early local care of the wound was deemed to be important mainly in a negative way. Usually some type of fixative, such as tannic acid (most frequently), gentian violet, dehydrated alcohol, trinitrophenol or aluminum acetate, was used, but not with the idea of the fixative being of great value in the correction of the disturbance in physiologic relations but because of the cleanliness of the method and the lessened disturbance to the patient.

As Taylor⁶ has noted, the too ambitious use of tanning solutions in cases of superficial burns may fix not only the dead layers of skin but any of the germinal layer and the appendages of the skin that may remain, such as the hair follicles or the sebaceous glands. To the fixa-

3. Berkow (A Method of Estimating the Extensiveness of Lesions [Burns and Scalds], Based on Surface Area Proportions, Arch. Surg. 8:138 [Jan.] 1924) has again within recent years emphasized that for the purpose of prognosis it is important for the physician to estimate at an early time the relative area of the body surface involved.

4. Smith, A. H., and Mendel, L. B.: The Adjustment of Blood Volume After Injection of Isotonic Solutions of Varied Compositions, Am. J. Physiol. 53:323-344, 1920.

5. Rowntree, L. G.: Water Intoxication, Arch. Int. Med. 32:157-174 (Aug.) 1923; The Effects on Mammals of the Administration of Excessive Quantities of Water, J. Pharmacol. & Exper. Therap. 29:135-159, 1926.

6. Taylor, Frederic: The Misuse of Tannic Acid, J. A. M. A. 106:1143-1145 (April 4) 1936.

tion method associated with Davidson's name⁷ there has been attributed by him and others⁸ a decrease in mortality principally during the second twenty-four hour period. In the cases considered in this paper a decrease in mortality during this period seemed to be associated rather closely with the proper systemic management of the patient rather than with the care of the local lesions.

When proper early precautions were taken the development of a true abscess beneath the tanned crust was of rare occurrence. When a collection of pus did occur, its appearance was noted usually at about the time that the separation of the dead soft tissues from the live tissues was nearing completion, i. e., about the end of the third week. Then a small incision through the crust or even the application of a dressing moistened with saline solution gave adequate drainage.

THE INTERMEDIATE PERIOD

In the series of cases reported here 93 thin grafts were applied to cover a granulating surface. These were applied on 59 patients at 80 separate operative procedures. The granulating areas covered averaged 89.6 sq. cm., and 32 of these were caused by a burn with an average area grafted of 93.6 sq. cm.

Relation of Area and Depth to Contractural Deformity.—The early recognition of not only the depth of epithelial destruction but the area of complete epithelial loss is an essential point that needs to be grasped by the surgeon if he is to develop a practical successful method of repair. In cases of burns of a degree (fig. 1) that destroy only a portion of the epithelial "pegs" within a period of from two to three weeks, reepithelization from below upward and skin grafting were seldom necessary. When all layers of the epithelium had been destroyed, the wounds tended to close by two methods: (1) by fibrosis and con-

7. Davidson, E. C., and Matthew, C. W.: Plasma Proteins in Cutaneous Burns, Arch. Surg. **15**:265-274 (Aug.) 1927.

8. Davidson, E. C.: The Prevention of the Toxemia of Burns: Treatment by Tannic Acid Solution, Am. J. Surg. **40**:114-116 (May) 1926; Sodium Chloride Metabolism in Cutaneous Burns and Its Possible Significance for a Rational Therapy, Arch. Surg. **13**:263-277 (Aug.) 1926; Tannic Acid in the Treatment of Burns, Surg., Gynec. & Obst. **41**:202-221, 1925. Glover, D. M.: Six Years of Tannic Acid Treatment of Burns, *ibid.* **54**:798-805, 1932. Harris, R. I., quoted by Davidson, E. C., and Penberthy, G. C.: Treatment of Burns in Children with Tannic Acid, Proc. Internat. Assemb. Inter-State Post-Grad. M. A., North America **5**:265-268, 1929. Herzfeld, G.: Treatment of Burns and Scalds by Tannic Acid, Practitioner **122**:106-111, 1929. Wilson, W. C.: The Tannic Acid Treatment of Burns, Medical Research Council, Special Report Series, no. 141, London, His Majesty's Stationery Office, 1929. Beekman, F.: Tannic Acid Treatment of Burns, Arch. Surg. **18**:803-806 (March) 1929. Bancroft, F. W., and Rogers, C. S.: Treatment of Cutaneous Burns, Ann. Surg. **84**:1-18, 1926; Arch. Surg. **16**:979-999 (May) 1928; New England J. Med. **202**:811-822, 1930.

traction of the granulating base and (2) by a slow scarred epithelization progressing centrally from the edges (fig. 2). The anatomy of the part very largely determined the tendency for the surface to close by the first or the second method. Thus, when the denuded area was over the side of the ribs or in the middle of the thigh, where the bony structures were strong and the soft tissues only moderately yielding, a greater part of the closure of a wound was made by the scarred epithelium, which, according to the natural rapidity of epithelial growth, grew in from the circumference. On the other hand, when the destruction of soft tissues was located in front or back of a joint which could be restricted in its normal radius of movement, the greater part of the

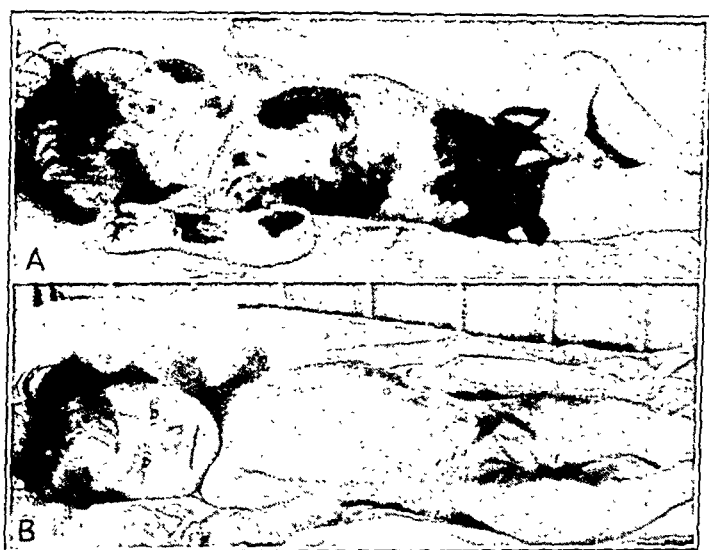


Fig. 1.—*A*, photograph of a rather superficial burn with fixative applied. In only one area (over the pubis) have all the layers of epithelium been destroyed. In a burn of this depth epithelization is quick because the new epithelium springs from the base. *B*, photograph of the same child taken three weeks after the burn.

wound closed by fibrosis, depending somewhat on whether the limiting scar was within or without the angle of movement. The larger the original surface destruction, the greater was the tendency to contracture and limitation of flexion or extension. In some instances an additional factor was added by the density and contractile pull of an innate tendency to the formation of a keloidal scar.

Preparation for Resurfacing.—By the end of the third week or the early part of the fourth week, when it was deemed that a well developed limiting wall of granulation tissue had formed, an abrupt change was made in the method of handling the local area. At this time the local burned area was wrapped within a wet thick gauze roll (fig. 3 *A*), which was reapplied twice daily and kept continuously wet. Early during this period, but not before, while the wound was being dressed

without anesthesia, gross dead tissues sometimes were cut away with scissors or a knife. When some difficulty or pain was experienced in removing the dressing, if the patient's condition permitted, the patient was placed in a tub bath (fig. 3 *B*) for fifteen or twenty minutes until the dressings fell off more or less spontaneously.⁹ Too long a period of immersion was found to be weakening in several instances,

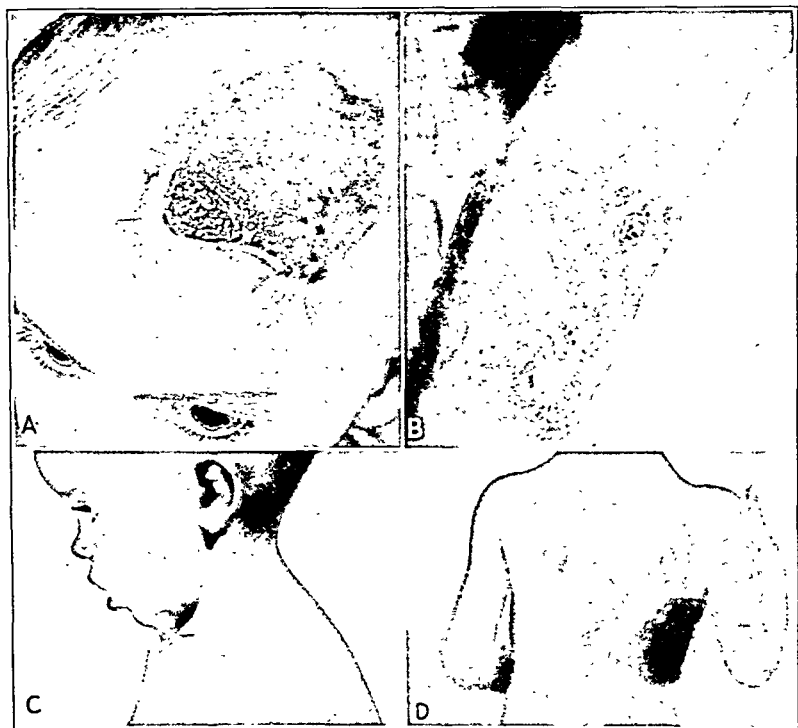


Fig. 2.—*A*, photograph of a burn, which if allowed to scar over without aid will be forced by the underlying anatomy to close principally by epithelization from the circumference. *B*, photograph of a burn, which because of the anatomy of the region has closed principally by epithelization from the circumference. *C*, photograph of a burn which has closed principally by the contracture of the fibrotic base. *D*, photograph of a burn which over the ribs will close principally by epithelization from the circumference and in the axilla principally by contractual fibrosis.

9. Paulus of Aegina, 629 to 690 A.D. (cited by Pack, G. T., and Davis, A. H.: *Burns: Types, Pathology and Management*, Philadelphia, J. B. Lippincott Company, 1930) is said to be the first to use the continuous water bath. Passavant (*Bemerkungen über Verbrennungen des menschlichen Körpers und deren Behandlung mit dem permanenten warmen Bade*, *Deutsche Klin.* 10:348, 365 and 373, 1858) first described and Hebra (*Ueber continuirliche allgemeine Bäder und deren Anwendung bei Behandlung von Verbrennungen*, *Allg. Wien. med. Ztschr.* 6:331 and 359, 1861) popularized the use of a continuous wet dressing.

and if the patient was showing considerable constitutional reaction immersion was not deemed advisable. Immediately after immersion a wet gauze roll was wrapped about the denuded area.

Saline solution was usually used, but at other times a saturated solution of boric acid or of magnesium sulfate was used. The particular solution used, provided it was not toxic, was not considered of great importance. The advantages of wet dressings were judged to be promotion of drainage, maceration at the line of demarcation, mechanical aid to the separation of slough and possibly some mechanical stimulus to the formation of a proper bed of granulation tissue. Moreover, the



Fig. 3.—*A*, photograph of the method of applying a wet roller gauze roll to a wound when the time has arrived for separation of the dead tissues from the live soft tissues. Sufficient cotton pads are placed between the gauze to hold the moisture well. Externally a layer of rubber surrounds the gauze to prevent too rapid evaporation. Periodically the gauze is remoistened. The roll is changed morning and evening. *B*, if much pain is complained of when the roll is removed, if the condition of the patient permits he may be placed in a tub immersion for a few minutes and the gauze removed under water either by the patient himself or by the intern. The simplest solution to use is hypertonic saline solution. Any antiseptic solution, if nontoxic, will act the same.

cleanliness of the method and the repetition of the dressing twice daily were regarded of importance in shortening the period necessary to give a proper granulating bed. Besides the general condition of the patient, the most important aid to early epidermization from the circumference of the wound was cleanliness (fig. 4 *A* and *C*). In the consideration of

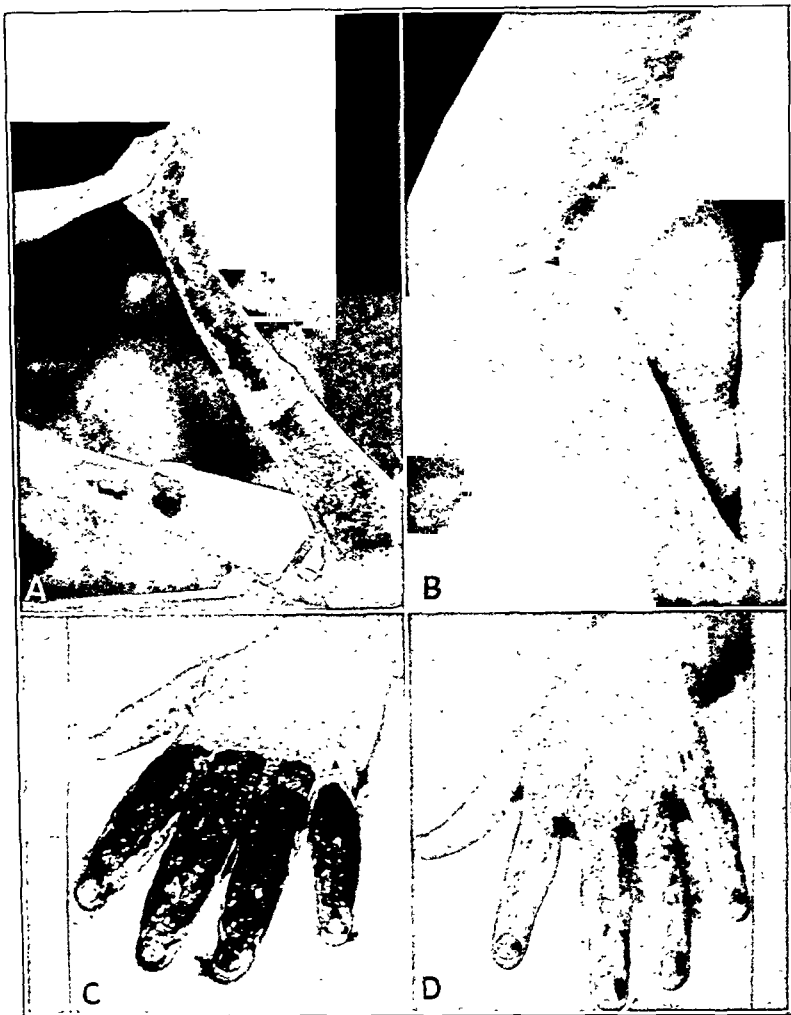


Fig. 4.—*A*, photograph of a large granulating wound of the leg of a patient ten days after beginning treatment by wet dressings and occasional tub immersion. She was burned thirty days before and was cared for at home by another physician, who used an ointment dressing which so far as the final result is concerned made little or no difference. An ointment dressing is, however, very “trying” on the patient and also on the one who has to do the dressing in the early days of the burn. A fixation method is a far more comfortable way of handling the situation. Whether or not it tends to prevent toxic absorption is quite another question. With the patient under gas anesthesia a large thin graft was applied from the opposite leg. Ninety per cent of the graft took. Thin grafts were taken from the inside of the left thigh, the outside of the right thigh and from the back. When taken along with the granulating area, owing to the burn such rather high percentage of body area was superficially denuded that about twelve hours after grafting skin from the inside of the right thigh, abdomen and back the patient showed signs of a mild “shock,” which was interpreted as due to too wide an area of denudation (granulating area plus weeping area from which skin had been removed). A blood transfusion corrected this. *B*, photograph of the legs one year later. Extension and flexion were normal. *C*, photograph of a granulating wound three weeks after infliction of a burn from a clothes mangle. The tendons were destroyed. A wet dressing was used for one week before the photograph was made. Thin thick skin was grafted. *D*, photograph of the hand six months later. The patient obtained perfect flexion after the application of a thin graft to the granulating surface. Such a pleasant result does not often occur if the burn is of somewhat greater depth because of fibrosis of the tissues about the phalangeal joints.

the general condition of the patient, the factor of a relative secondary anemia was found to be important both as to the rapidity of epidermization and as an influence in obtaining a proper granulation bed on which a graft would "take." When the granulations were exuberant, a rather firm tight bandage aided in getting a firmer base. When evidence of anemia was present, a blood transfusion was given.

*Grafting of Thin Skin on a Granulating Surface.*¹⁰—The appearance of the granulating surface was used as the index to the time of grafting. The proper appearance was judged to be present when the surface was free from evidence of grayish slough or any gross pus and the granulation base was firm but not too exuberant or watery and was cherry red. Bacterial counts on smear were not considered of particular value. Anemic persons did not present granulation surfaces of the proper texture or color. Whenever grafting was attempted without the criteria being fulfilled, at least a part and usually most of the graft failed to "take." On the other hand, when it was present, practically in 100 per cent of the cases 90 per cent or more of the graft "took."

After laying the graft on the granulating surface, the same type of thick roller gauze dressing was applied as previous to grafting. This dressing was not changed for four or five days, and during this time it was kept saturated with saline solution or a saturated solution of boric acid. When the graft was located so that articular or muscular movement would probably cause it to slip, either stitches or a splint of some type or both were used so that fixation was definite.

A factor of particular interest to the surgeon is the reason for failure of a graft to "take." Of the 93 grafts applied to cover a granulating surface, in 42 there occurred a "take" of 90 per cent, which may be considered as practically perfect; in 13 there occurred a "take" of over 80 per cent, which may be considered as "good," and in 30 there occurred a "take" of over 70 per cent, which was usually sufficient so that further grafting to the granulating surface was not necessary. In 8 the loss ranged from 30 per cent to loss of the entire graft. The usual cause of loss was infection developing beneath a part or all of the graft. This usually was due to desultory preparation of the granu-

10. Possibly rather arbitrarily, a thin graft, to my mind, has been defined as any graft that leaves a part of the epithelial "pegs" in the area from which it was removed so that new skin regenerates from the bottom and the wound does not heal by growing in from the sides. Included in this definition would fall the "Thiersch" graft (Thiersch: Arch. f. klin. Chir. 17:318, 1874) and the so-called "split" graft (Blair, V. P., and Brown, J. B.: The Use and Uses of Large Split Grafts of Intermediate Thickness, Surg., Gynec. & Obst. 49:82-97, 1929) which is alleged to be a thicker graft than the Thiersch graft. At least the split graft places emphasis on the advantage of cutting a thick graft rather than a thin one.

lating surface, along with an error in judgment as to the time when the surface was in condition to receive a graft. In a few instances, improper fixation was the basic fault.

In patients on whom the skin was grafted when the hemoglobin content was below 65 per cent it was estimated that the chance of a



Fig. 5.—*A*, photograph of a granulating wound and cicatrix caused by an electrical burn inflicted eighteen months previously. The attachment of the triceps muscle to the olecranon had been destroyed. The patient could flex his arm by use of his biceps, and gravity caused extension. *B*, photograph of the front view of the healed cicatricial contracture of the axilla. *C*, photograph a few weeks after the application of a "split" graft to the axilla and to the granulating wound about the elbow. A little over 45 degrees of flexion was present.

successful "take" with a thin graft on granulating surface was decreased from one-third to one-half because of a greater tendency for the graft to be destroyed by infection.

When the granulating base was relatively new, a large thin graft showed a greater tendency to "take" well if the granulation tissue was not interfered with, but when sufficient fibrosis had occurred to give a firm scar base the chances of a complete "take" with a thin graft after the granulation and a part of the yellow scar base were sliced off were not decreased, and often some of the contracture was relieved, and better functional and cosmetic results were thereby obtained.

In several instances in which the patient was seen for the first time several months after the original injury and healed contractures had formed but part of the surface remained unhealed (fig. 5), it was often possible not only to cover the granulating area with a thin graft but to cross cut the contracture and largely correct the contractural deformity. In cases in which the contracture was graver, deformity was not always prevented, and the cosmetic result on such areas as the neck and face was often definitely unsatisfactory. Moreover, on such regions as the palm of the hand, the front of the leg and the bottom of the foot the amount of protection which a thin graft offered to the underlying tissues was not sufficient.

THE CORRECTION OF CICATRICAL AND COSMETIC DEFECTS AFTER COMPLETE HEALING

For the coverage of a fresh raw surface, I have used 165 thin grafts on 98 persons at 118 separate operations and 256 full thickness grafts¹¹ on 127 persons at 163 separate operations. Of the former grafts, 87, covering an average area of 29.5 sq. cm., were applied on 45 persons at 58 separate operations, and of the latter, 155, covering an average of 26.4 sq. cm., were applied on 67 persons at 91 separate operations to correct a healed cicatrix following a burn.

Chance of Failure of Graft to "Take."—Fortunately one seldom has to contend with the chance of not getting a good "take" when using a thick skin graft for the correction of a healed defect. When a full thickness graft is used to correct a healed defect, unfortunately one has to consider the possibility of a partial or even a complete failure to obtain a good "take." Of the 155 full thickness skin grafts used to correct the damage resulting from a burn, 130 showed (from 95 to 100 per cent) good "takes," which meant that a surgically clean surface was obtained, that the hemostasis was adequate, that the proper tension of transplanted skin was obtained, that the proper pressure was applied

11. A full thickness skin graft (Wolfe, J. R.: *New Method of Performing Plastic Operations*, Brit. M. J. 1:360, 1875) is a free transplant which usually leaves no part of the epithelial "pegs" in the area from which it is removed. Section is made across the lower third of the corium. Unless the resulting wound is drawn together by sutures, the defect closes by a combination of fibrotic contracture and scarred epithelization.

to gain coaptation between the graft and the bed and that adequate fixation or splinting was provided. In 3 instances the whole graft was lost. In 25 instances the loss was partial and ranged from 10 to 90 per cent. The causes of the loss were judged to be infection of all or of some part of the grafted area in 12 cases, lack of adequate pressure in 12, too much pressure in 1, blood clot in 2 and improper splinting which allowed muscular movement beneath the graft in 1.

Average Final Contracture of the Grafted Area.—Provided a good "take" occurred, the most important influence on functional result was the final amount of contracture of the grafted area. The subsequent average contracture of the full thickness skin graft when used in the correction of the damage resulting from a burn averaged 17 per cent and of the thin graft, 38 per cent.

Dressing for Grafts on Fresh Raw Surfaces.—As a rule, a graft applied to a clean raw surface was fixed by stitches, whether or not a thin or thick graft was used, a dressing of gauze treated with 5 per cent bismuth tribromphenate in petrolatum was laid on the graft and then a moderately thin layer of gauze was applied. Finally, a damp marine sponge was compressed by a bandage or stitches or both over the graft (fig. 6 *A* and *B*).

When movement seemed an eminent factor, some type of fixation by splinting was added. Externally, when the anatomy of the location was such that an outlay wax stent (fig. 6 *C*, *D* and *E*) gave better chances of the proper amount of pressure and tension on the graft, the tissue to be grafted was stitched about a wax form. Internally, within the mouth, as a rule, a wax stent was used.

The Selection of the Type of Graft.—My judgment as to the better type of graft to apply to a given region¹² under a certain group of circumstances has undergone considerable revision from time to time. Usually the ideal objective was balanced against the probability or the possibility of attainment in a reasonable manner.

When one wishes to correct a contracture about such a region as the axilla, the popliteal space or the elbow, full movement of the extremity is the first consideration. In the axilla it was found that a good "take" with a full thickness skin graft is somewhat difficult to obtain because of the likelihood of not getting uniform pressure. One does not encounter this difficulty about the elbow or the popliteal space. A proper amount of a thin graft will usually correct an axillary contracture (fig. 7 *A* and *B*). As this graft is the most certain to grow and the postoperative period of dressing is short, after making use of

12. Padgett, Earl C.: Full Thickness Skin Grafts in the Correction of Soft Tissue Deformities, *J. A. M. A.* 98:18-23 (Jan. 2) 1932; Early and Late Treatment of Burns, *J. Kansas M. Soc.* 34:184-188, 1933.

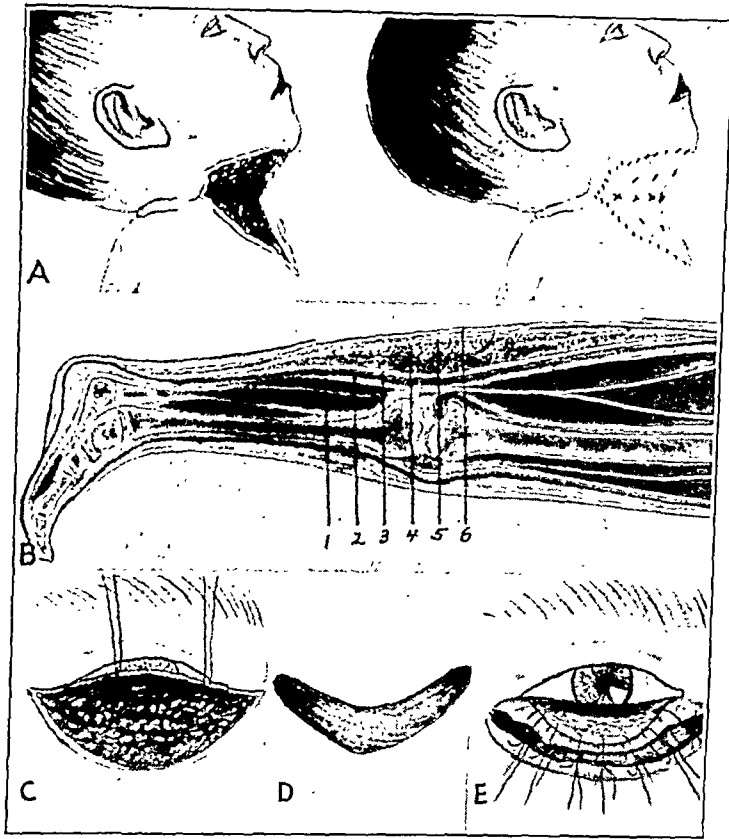


Fig. 6.—*A*, diagram of the method of cross-cutting a contracture and getting overcorrection. In this diagram a full thickness graft is shown stitched in place. In the gutter a few stitches were placed to aid in fixation. A few stab holes were made to prevent accumulation of fluid beneath the graft. When a thin graft was used the stitching was similar but looser, and the graft was made to overlap the edge of the skin. When more than one graft was used to cover the raw area, the grafts were overlapped and stitched through and through to the base beneath. *B*, diagram to illustrate the layers of the dressing: 1, the graft; 2, layer of bandage gauze impregnated with 5 per cent bismuth tribromphenate in petrolatum; 3, thin layer of wet gauze; 4, thick overlapping layer of marine sponge; 5, moist cotton pad and firm bandage; 6, possibly some type of splint to prevent movement. In this case an external cast was used. Often no splint is necessary. Whether a splint is needed for fixation depends on the location. *C*, diagram of an ectropion of the lower eyelid caused by a cicatrix which has been corrected by a lengthwise incision just beneath the eyelashes and cross-cutting of the cicatricial bands. *D*, diagram of a stent made of dental modeling composition before insertion over the muscle of the lower eyelid. *E*, diagram showing a method of wrapping a thick thin graft or a thin full thickness graft about the wax stent; by means of interrupted silk stitches pulled snugly over the stent the graft has been placed on tension and pressure given so that firm contact with the raw base is obtained. From 30 to 50 per cent overcorrection is made to allow for subsequent contracture.

any material available for a switch pedicled flap, a thin graft was usually used for the remainder of the raw surface in the axilla. The same was applied to perineal contractures. About the elbow and about the popliteal space, groin or back of the hand both types of grafts have been used, but because of the lesser tendency to contracture the full thickness graft was more often given the preference (fig. 8 *A* and *B*).

In cicatricial contracture of the palm of the hand (fig. 8 *C*, *D* and *E*) and the flexor surfaces of the fingers, the full thickness skin graft offered on the average a good functional result. Although a good

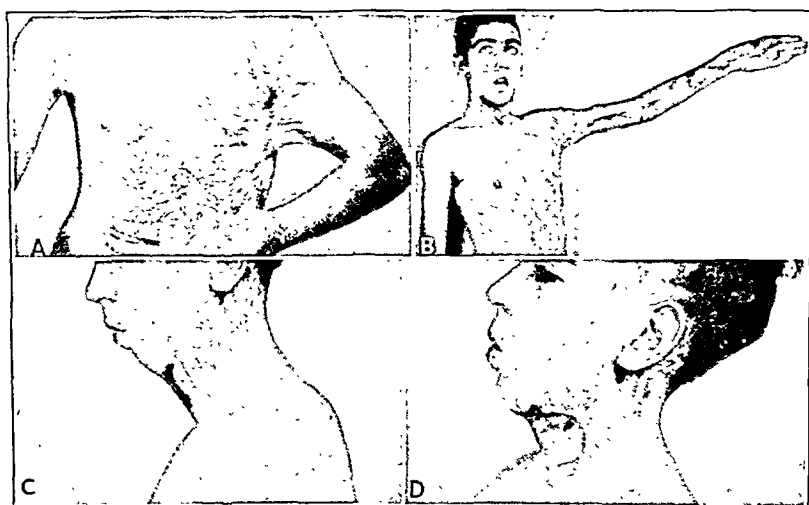


Fig. 7.—*A*, photograph of a healed cicatricial contracture of the left axilla, neck and thumb. *B*, a so-called "split" graft (a thick thin graft) was used for correction of the axillary contracture after cross-cutting the contracture. The photograph was made six weeks after the patient left the hospital. He was seen six months later, and the correction was complete. A full thickness graft was applied over the left thumb contracture. *C*, photograph of a neck contracture. The contracture was cross-cut, and a full thickness graft from the thigh was applied. As the patient was a boy and a collar would be worn it was considered that the essential factor was functional correction. *D*, lateral view of the neck six weeks later.

"take" was more certain and the subsequent period of dressing was shorter, the thin grafts on the ventral surface of the fingers (fig. 9) between the fingers and over the dorsum of the hand usually did not give as satisfactory a result as did the thicker graft. The final contracture was greater, the appearance was not so near that of normal skin and in the case of ventral surface of the fingers the protection

was not always adequate. The full thickness skin graft in the palm of the hand gave a good result functionally and cosmetically. The ultimate contracture was not so great that it could not be compensated for at the time of the operation, and the protection was adequate. After a graft was applied, some type of splint to hold the fingers of the hand in a position of overcorrection for several weeks aided the result very materially.

On the anterior portion of the neck a thin skin graft, although almost certain to "take," usually contracted from 50 to 70 per cent, too greatly to correct the contracture, and the appearance usually was not

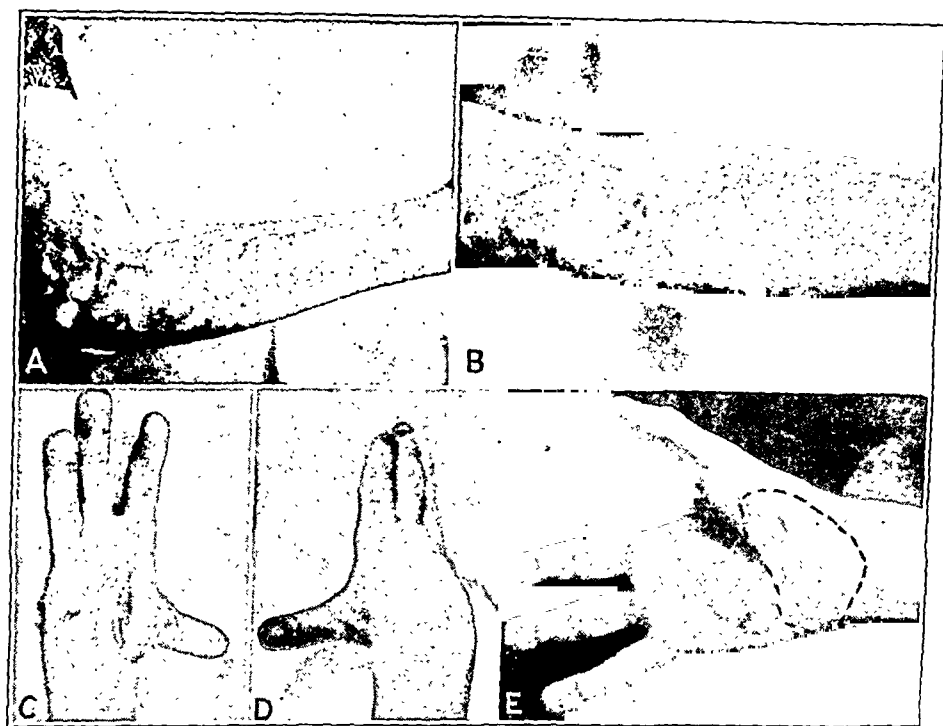


Fig. 8.—*A*, photograph of a contracture of the region of the elbow. *B*, photograph made two months after release of the contracture and application of a full thickness skin graft. *C*, photograph of a contracture of the palm of the hand, palmar view. *D*, dorsal view of the hand. The little finger was removed at some previous operation. The contracture was cross-cut, and a full thickness skin graft was applied. *E*, photograph of the preceding hand eight months later. The graft lies within the dotted line.

satisfactory. In over 80 per cent of the attempts a good "take" after the application of a full thickness skin graft to the upper and anterior portion of the neck was obtained. When this occurred the contracture was corrected in from one to two operations, and the cosmetic result was good. The swallowing movement usually caused some loss of a

graft over the thyroid cartilage no matter what type of dressing was used with the idea of preventing it. In later cases an attempt was always made not to leave a raw area over this region.

After both thin and full thickness grafts had been tried out over the thyroid cartilage, the adjacent sides of the cheek and the mandible, it was found that the latter usually was given the preference, because the full thickness graft more nearly approximated the normal skin in appearance (figs. 10, 11 *A* and *B* and 12). On the sides of the face the full thickness graft has been given a decided preference. In these regions the final result after a satisfactory "take" of a full thickness graft justified the risk of not getting a good "take." Some of the most

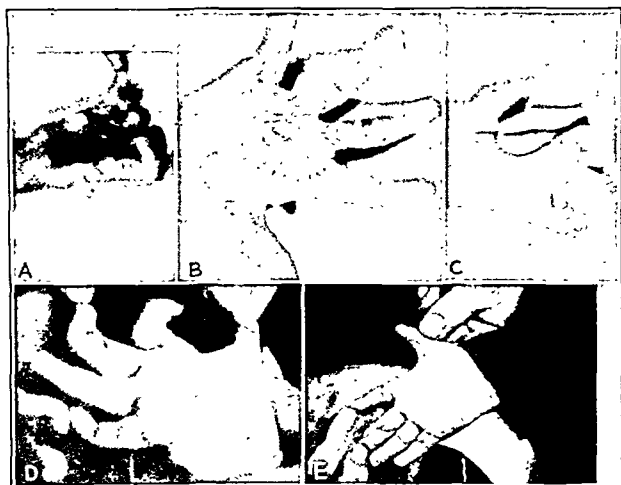


Fig. 9.—*A*, photograph of a ventral cicatricial contracture of the fingers of the right hand. The scar was cross-cut, and a full thickness skin graft was applied. *B*, a photograph three months later showing extension. *C*, made at the same time, shows flexion. *D*, contracture of the thumb and first finger. The contracture was cross-cut, and a full thickness skin graft was applied. *E*, a photograph made three months later.

brilliant results were obtained with large full thickness grafts to the face. Although in several instances the appearance of the graft was somewhat whiter than normal skin, a thick thin graft gave a satisfactory result when applied over the orbicularis oris muscle for an ectropion of the upper or the lower lip.

When a full thickness skin graft was used on the neck and chin, about the mouth and over the cheek, in at least half of the cases a secondary operation was found to be necessary after a period of several months, for the purpose of excising the rather heavy scar which often

forms at the juncture of a full thickness skin graft with the surrounding normal skin. Moreover, even in advent of obtaining a good "take" of a full thickness skin graft on the face, the possibility had to be considered of having the graft appear too shiny or in brunettes of presenting a discoloration from pigmentation. Although there was a tendency for the full thickness graft to have a slightly shiny appearance, most of the grafts that "took" well without much superficial exfoliation eventually showed grossly almost the normal texture of the skin of the region from which the graft was removed. Those grafts in which

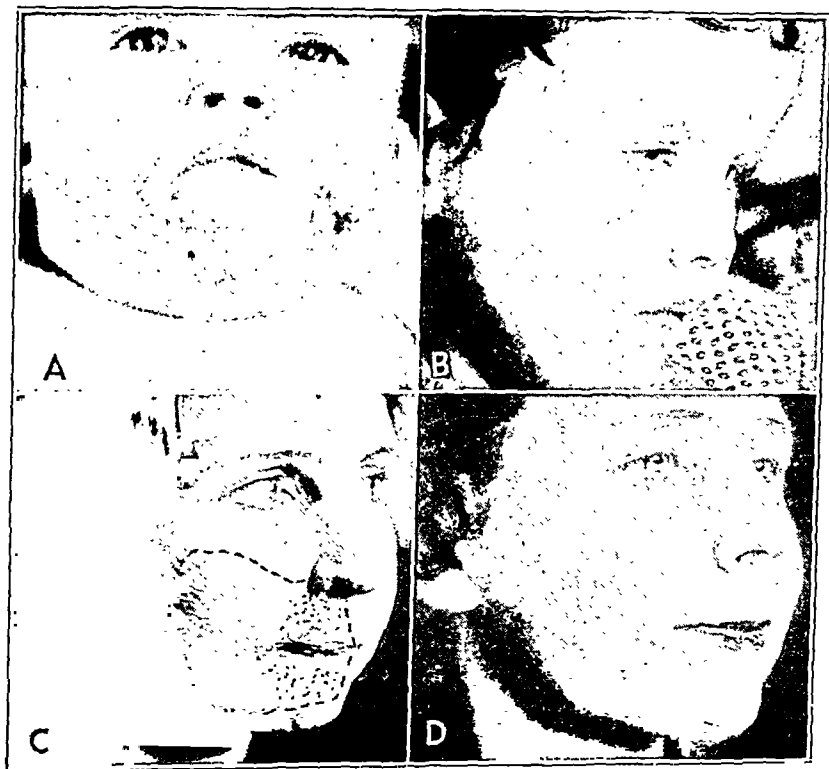


Fig. 10.—*A*, photograph of a cicatricial keloidal contracture of the side of the face. The scar was removed, and a full thickness skin graft was applied. *B*, a photograph made two years later. *C*, photograph of a scar of two thirds of the side of the face and extropion of the upper and the lower lid. A full thickness skin graft was applied to the side of the face. The dotted outline shows the extent of the scar. Over the dotted area on the region of the upper and the lower lip a heavy split graft was used. *D*, photograph of the final result two years later after excision of surrounding scar.

some superficial exfoliation occurred had more of a tendency to show pigmentary changes. In pronounced brunettes, pigmentation sometimes occurred in a perfect "take."

On the sides of the neck, over the sternocleidomastoid muscle and the posterior portion of the neck a thin graft was found to give

an acceptable result functionally and cosmetically. Here the contracture was usually less than one-third. Because of the ease of application and the certainty of a "take" in this region, the thin graft was given preference.

When a muscle was near the surface, as about the eyelids (fig. 11, *C* and *D*), about the lips or over the sternocleidomastoid muscles on the side of the neck, the results obtained after the application of a thin graft were as good or in rare instances even better than that after obtaining a good "take" with a full thickness graft. When such is the case, the greater likelihood of a perfect "take" after the application of



Fig. 11.—*A*, a photograph of a large hemangioma of the face which had been burned by the x-rays and radium. The area showed telangiectasis and mottled and scaly patches. Complete removal was carried out, and a large full thickness skin graft was applied. *B*, a photograph of the result one year later. *C*, a photograph of ectropion of the lower eyelid with destruction of the outer canthal region. The scarred side of the face is shown by the dotted outline. After excision of the whole scar, a large heavy split graft was applied to the temporal region and the side of the face and a thick thin stent graft was used over the eyelids. *D*, a photograph of the result two years later.

a thin graft, the shorter period for postoperative dressing and the probability of only a slight cicatrix at the junction of the graft with the normal skin speak strongly in favor of the thinner graft. For this reason about the eyelids most often a relatively thick thin graft draped about a wax form was used, but more rarely a thin full thickness graft

from back of the ear was used. Probably the latter method most nearly approached the ideal about the eyelids.

Acceptable eyebrows were made with a full thickness graft from the scalp. The hair was found to be somewhat sparse and less plentiful than in a normal scalp, but with care in clipping the new eyebrow was fairly successful.



Fig. 12.—*A*, a photograph of a severe burn with a partially healed cicatrix. Multiple skin grafting operations were carried out after the contracture was cross-cut, which was to be corrected at the given operation. Note the contracture of the neck, about the lower lip and axilla and over the groin. The right thigh was pulled into a position of nearly 45 degrees flexion. The boy lay in bed in an almost vertical ball. A "split" graft was used for the axilla and the right groin. Full thickness grafts were used for the neck and chin, beneath the lower lip and behind the right ear to release it from his head. *B*, a photograph of the general result eighteen months later.

THE PRACTICABILITY OF HOMOGRAFTING

In 1932 I published my results with 44 experimental isoskin grafts, or homografts.¹³ Since that time the experiment has been repeated in

13. Padgett, Earl C.: Is Skin Grafting with Isografts or Homografts Practicable, *West. J. Surg.* **41**:205-212, 1932; Is Skin Grafting with Isografts or Homografts Practicable? *Surg., Gynec. & Obst.* **25**:786-787, 1932.

6 cases. My data show that the result to be expected after isodermic transplantation by ordinary methods, at least, may be summarized as follows: An immediate "take" occurs in the majority of cases. In nonrelated persons, between the second and the third week the grafts begin to disappear, and by the end of the fourth week they have completely disappeared. In persons related by blood (syngenesiotransplantation), such as father and son or even uncle and nephew, the grafts "take" and remain viable about three weeks, but by the end of the fifth week they are destroyed. In identical twin transplantations (the closest possible syngenesiotransplantation or "near relation transplantation") the grafts may remain. Syngenesiotransplantation of skin is theoretically improbable except in identical twins, in whom it is theoretically probable and clinically has occurred. The failure of experimental isodermal grafts on man and on animals to remain viable or to show a relationship to the blood group in the length of time viability is present and theoretical reasoning argue against the blood group of the patient as playing a rôle of any essential significance in homotransplantation of the skin. The bulk of experimental and clinical experience is in agreement that isotransplantation or homotransplantation of skin is not practicable except possibly in identical twins. Thus, some antagonism not as yet understood apparently exists between the cells of the host and the donor, even in close relatives, and as the distance of the relationship within the species is increased progressively the antagonism is more marked. Moreover, without species the antagonism is even more marked than within species. The great importance of the relative nearness of the relationship of the genes of the host and the donor of the transplant is apparently the crux of the matter.

SUMMARY

Of a series of 514 skin grafts transplanted at 361 separate operations on 257 different persons, 299 were transplanted at 193 separate operations on 144 persons to alleviate a burn.

To exemplify the problems encountered in the care of a severe burn in the early, the intermediate and the late stage, a series of 144 burned persons was found to present the necessary situations.

In the care of the severely burned greater emphasis should be focused early on alleviation of the profound systemic disturbance than is placed on the care of the local lesion.

The recognition of the depth and the area of complete epithelial destruction is an essential point to be grasped if one is to understand the principles of reepidermization and the basic cause of contractural deformity.

Early resurfacing after a large complete loss of skin should always be the goal of the efficient surgeon because of the decrease in the

period of convalescence with its economic potentialities and the prevention of contractures with the functional incapacitation which accompanies them.

Provided the general condition of the patient is good, one's success in growing thin skin grafts on a granulating surface is directly proportional to the general cleanliness of the surface.

In an anemic person the chance of a good "take" on a surface of granulation tissue is decreased.

In the successful grafting of skin dependence on simple fundamental principles and methods, in contradistinction to a special type of graft with or without a "far-fetched" method of placement or puncturing or dressing, is important.

In the correction of cicatricial defects after complete healing has occurred, the decision whether to use a thin graft or a full thickness graft depends on a careful balancing of the characteristics of the two grafts, the main object to be attained in a given region and the relative risk of failure to get a good "take." Sometimes the disability entailed in the removal of the graft and the length of the period of postoperative dressing also become factors to be considered.

After observing a series of 50 experimental homotransplants in man, the conclusion was reached that isodermal grafting is not a practicable procedure unless an identical twin is available.

ABSTRACT OF DISCUSSION

DR. G. B. NEW, Rochester, Minn.: As Dr. Padgett has brought out, the treatment of extensive burns should always be considered an emergency of the greatest importance. To obtain the best results, treatment should be directed as soon as possible by the combined efforts of a team consisting of an internist, a biochemist and a surgeon.

In a recent symposium, Osterberg showed that the clinical picture observed in cases of extensive burns is due to excessive concentration of the blood with its resultant phenomenon and not to specific toxins produced as a result of the burning of the tissues. Bannick and Keith emphasized the necessity in cases of extensive burns of early relief from pain by the administration of morphine in order to prevent shock and of relief from marked dehydration. They urged that fluids be replaced early by sodium chloride and dextrose solutions.

The surgeon must cover the raw surfaces with a tannic acid spray as soon as possible. Seeger, however, has shown that there is no reduction in the ultimate mortality which can be attributed to the use of tannic acid, other factors in the treatment being comparable. The mortality has been reduced in the first five days, many of the patients dying, however, in the later stages. Of 369 cases of burns in the Milwaukee Children's Hospital, 39, or approximately 11 per cent, were fatal; of 197 cases in which tannic acid was used, 23, or 12 per cent, were fatal; of 172 cases in which other methods of treatment were used, 16, or 9 per cent, were fatal.

Brown and Blair's excellent work on the use of baths of hypotonic saline solution and early covering the raw areas with shaved skin grafts has been one of the most striking advances that I have seen in the treatment of burns. The

type of skin grafting employed must depend on the usual factors in determining the use of skin grafts in general. When the granulated area is ready for grafting, a shaved graft will cover the area with a high percentage of "takes," but when such a graft is used about the face and neck, there is usually a great deal of contraction, and the color is frequently not satisfactory. A secondary free full thickness skin graft or a skin flap becomes necessary. When a full thickness skin graft is used about the cheeks, submental or submaxillary region, wiring the upper and the lower teeth together as one would in a fracture of the lower jaw, the patient being fed with a Rehfuess tube, prevents any movement, thus adding considerably to the percentage of "takes." A free full thickness skin graft is best used over the muscles of expression, as it is almost impossible to get a flap thin enough so that the muscles show through. The color, of course, in the flap is much more satisfactory than can be obtained by a shaved or free skin graft. A large tube flap taken from the chest with one pedicle in the infraclavicular region and the other well down on the chest gives excellent results. The area in the infraclavicular region simulates closely the skin of the face and neck in color and texture and makes ideal material for this purpose. The lower end of the tube flap on the chest is carried to the neck or region of the mastoid, and then the skin in the infraclavicular region is carried to the neck or face where it is to be utilized. If the full thickness of the nose or cheek has been destroyed, it is necessary to line the area in the infraclavicular region with a full thickness skin graft in order to prevent the transferred skin from pillowing. In the cases with scarred band contractions, the use of the Z or VY incision operation will release them and correct much of the deformity. Dr. Padgett's results in this work have been extremely good, and he should be highly complimented.

DR. JAMES BARRETT BROWN, St. Louis: Although there are many reports on the treatment of burns, the small number of authors who publish final results as to healing and function in large series of patients who have lost the full thickness of the skin over a wide area is small. The late care and repair in such cases may require more time-consuming and exacting work than the primary treatment.

When deep burns heal there are contractions of the surrounding tissue and final closure of the defect by "scar" epithelium growing in from the sides. This scar epithelium is thin, contains no hair or sweat glands and lies flat on fibrous scar tissue that has no papillary layer or other semblance of normal derma. This condition does not change throughout years except that there may be some softening. There may be a general shortness of the skin necessary for function; over weight-bearing areas there may be chronic ulceration, and in any area this thin scar epithelium is subject to rapid and wide loss from infection or trauma. Microscopic studies of a large number of scars have shown this plainly, and on several occasions I have taken specimens for biopsy from areas that have been traumatized and have found the entire "scar" epithelium grossly dissected loose from the underlying fibrous tissue by hemorrhage.

The substance of the care of areas in which there is an extensive loss of the surface is that they should be repaired as soon as possible with skin grafts. The main difference in my method of repair in such cases from that discussed by Dr. Padgett is that I limit the number of full thickness skin grafts and substitute a graft that includes from one third to three fourths of the thickness of the derma. This graft might be called a thick Ollier-Thiersch graft, but the term thick split graft may be used to identify it from the thin, almost useless Ollier-Thiersch graft and from the full thickness graft.

The thick split graft may be cut rapidly and easily in large pieces and will "take" almost as successfully as the thin Ollier-Thiersch graft. It does not give

as good immediate result as the full thickness graft, but it may be risked on open wounds, and perhaps its greatest advantage is that healing of the site from which the graft is taken occurs rapidly, in contradistinction to the great trouble experienced in getting the sites from which large full thickness grafts are taken to heal. I have grafted 173 square inches of this type of graft at one time. Healing progresses toward the surface from the deep glands in the derma, and microscopic studies have shown complete surface coverage as early as the sixth day. This process is a "dedifferentiation" of the epithelial cells and progresses in the opposite direction of the growth of a cancer. A semblance of the picture of actual cancer may occasionally be seen in examination of this surface healing process in different stages.

One of the main uses of this type of graft is in effecting major repairs with a minimum of time and operations. The repair of badly contracted axillary and popliteal regions seldom requires a full thickness graft or pedicle flap, and, at least for the primary release of contractures about the neck, the thick split graft may be used to get the head up and the mouth closed and to allow the patient to resume a normal social and economic status. Then, if there is too much roughness or recurrent deformity, any other method of repair may be used.

DR. EARL C. PADGETT, Kansas City, Mo.: Possibly I have favored the full thickness skin graft a trifle more than is necessary. A certain amount of idealism has entered into the matter. When a good "take" of the full thickness graft is obtained, it undoubtedly in certain instances has qualities superior to those of any other graft. This is true especially for the face and neck. It would seem that with the use of a procedure with which one can succeed completely in 80 per cent of the attempts and can obtain partial success in another 15 per cent of trials, if a little more could be learned of the reasons for failure and certain adverse factors eliminated, one should succeed in nearly 100 per cent of the trials. I have succeeded in obtaining a good "take" in 5 cases of hemangioma of about one half of the face. Such an operation is heroic, but in adults I believe that it gives a result when successful which cannot be approached by other methods. An occasional failure in growing a full thickness skin graft, however, must be expected. I have had a failure after excising a large cicatrix of the face following a burn. The principles that make for success are the same, however, after excision of either lesion—a cicatrix or a hemangioma.

SURGICAL DISEASE OF THE GALLBLADDER

CLINICAL AND PATHOLOGIC REVIEW OF THE DISEASE IN 133
PATIENTS OPERATED ON AT THE MOUNT SINAI
HOSPITAL, WITH FOLLOW-UP STUDIES

DAVID R. MERANZE, M.D.

Pathologist and Director of Laboratories

HARRY A. SALZMANN, M.D.

Associate, Surgical Service No. 2

AND

THEODORE MERANZE, M.D.

Assistant Pathologist

PHILADELPHIA

The incidence of disease of the gallbladder in the adult population, the term being limited to include calculous and noncalculous cholecystitis, is very high. Stewart, of the University of Leeds, is quoted by Blackford, King and Sherwood (cited by Palmer¹) as reporting evidence of disease of the gallbladder in 16.4 per cent of 6,000 routine autopsies. Blackford and his associates concluded that more than half of the adults past 30 years of age have abnormal gallbladders and that approximately one fifth of these have gallstones. According to the statistical studies of Graham and his co-workers (cited by Hauser²), from 20 to 25 per cent of all adults have gallstones and probably an equal number have cholecystitis without stones. Thus, about 40 per cent of the adult population have disorders of the biliary system, which in probably the majority of instances are at times associated with more or less severe symptoms. McEvedy³ found that calculi are absent in 20 per cent of persons with definite cholecystitis, whereas in a small percentage of patients with gallstones the gallbladder shows no definite change or evidence that the inflammation has followed the calculi. Moynihan (cited by Burton⁴) said that "all gall-stones except pure cholesterin calculi invariably cause symptoms."

From the Laboratories and Surgical Departments of the Mount Sinai Hospital.

1. Palmer, W. L.: Gall Bladder Disease: Remarks on Symptoms, Diagnosis, and Treatment, *Internat. Clin.* **1**:111-123 (March) 1935.

2. Hauser, H.: Practical Application of Cholecystography, *Radiology* **21**: 472-477 (Nov.) 1933.

3. McEvedy, P. J.: Gall Stones and Cholecystitis, *Clin. J.* **64**:111-115 (March) 1935.

4. Burton, J. A. G.: Cholelithiasis: A Summary, *Glasgow M. J.* **121**:14-23 (Jan.) 1934.

Although the literature is replete with clinical reports and follow-up studies of cases of disease of the gallbladder, there have been few studies dealing with the relationship between the pathologic changes found at operation, the results of the histologic study of operative specimens and the clinical course in any particular series of cases of this disease. In the present study it has been our purpose to correlate the histologic structure and the gross pathologic picture of the gallbladder found or removed at operation with the clinical symptomatology and the subsequent results of operative treatment in those cases in which follow-up studies were possible. With this in view, we have made a complete and careful study of 133 patients with disease of the gallbladder who were treated at the Mount Sinai Hospital from 1930 to 1935. Follow-up data were obtained in 61.6 per cent of the group. Patients with malignant growths of the biliary tract or persons who were not operated on were not included. The results thus obtained have been critically correlated with the histopathologic picture. Coincidentally, an attempt has been made to analyze the causes of morbidity and mortality with the purpose of recognizing pathologic conditions corresponding to the clinical course.

The controversy over the advantages of cholecystostomy as compared with cholecystectomy seems at present to have abated, but it is by no means conclusively settled. Surgeons now agree that an infected gallbladder is incapable of being restored to normal function (Graham⁵) and may also act as a focus of infection. Moreover, the degree of disability which a patient suffers as the result of a diseased gallbladder is dependent not only on the changed content of the gallbladder and the involvement of its wall but on the associated involvement, for which the diseased gallbladder may be in part responsible, of the pericholecystic structures, i. e., the liver, pancreas, duodenum and common bile duct.⁶

Hartmann, Alvarez, Deaver, Zinc and others (cited by Mackey⁷) concluded from their findings that the results of cholecystectomy in cases of cholecystitis without stones are better than the results in cases of frank cholelithiasis. They explained their findings by the assumption that cholecystitis without stones represents the earliest stage of disease of the gallbladder and expressed the belief that when the stage of cholelithiasis has been reached there have developed, in a large proportion of cases, lesions in other viscera, which persist after cholecystectomy

5. Graham, R. R.: *Surgical Therapy in Gall Bladder Disease*, Canad. M. A. J. **30**:119-123 (Feb.) 1934.

6. Deaver, J. B.: *Causes of Morbidity and Mortality of Operation for Gall Stone Disease*, Surg., Gynec. & Obst. **49**:308-315 (Sept.) 1929. Graham.⁵

7. Mackey, W. A.: *Cholecystitis Without Stone: Investigation of Two Hundred and Sixty-Four Operated Cases from the Clinical, Radiological, and Pathological Aspects*, Brit. J. Surg. **22**:274-295 (Oct.) 1934.

and continue to cause symptoms. On the other hand, Flörcken, Gundermann, Seuleberger, Hitzrot and Cornell, Müller, Lahey and others (cited by Mackey⁷) found that the clinical results of cholecystectomy were better in cases of cholelithiasis. In many cases in which the stoneless gallbladder was removed at operation but symptoms have persisted, they argued that the gallbladders have not been the cause of the symptoms with which they have been libeled. On the basis of a statistical study, Peterson⁸ stated that favorable results were obtained with cholecystectomy in cases of cholecystitis associated with stones, i. e., cure in 83 per cent, while in cases of cholecystitis without stones the operation resulted in cure in only 52 per cent. Cholecystostomy alone in cases of each type resulted in a cure in 52 per cent. Mackey,⁷ after reviewing 6,000 cases reported in the literature, summed up the evidence obtained as follows: "The experience of a large number of surgeons in the past has shown that cure or improvement after cholecystectomy may be expected in nearly 90 per cent of cases of cholelithiasis and in nearly 80 per cent of cases of cholecystitis without stones." Others like Judd and Priestley and Hueck (cited by Mackey⁷) could find no appreciable differences in the results following operation in these two types of cases.

In our group of patients there were 15 with cholecystitis without stone formation who came to operation. Of this number, follow-up information was obtained on 7. Mackey,⁷ in a similar study, found that the results were usually more gratifying in cases in which the clinical symptoms were well marked than in those in which the symptoms were not marked. It appears also that the removal of those gallbladders which presented definite pathologic changes yielded better clinical results than excision of gallbladders in which the pathologic changes were minimal.

Since our group of patients with noncalculous cholecystitis is small and the results obtained by study were in agreement with those reported by Mackey,⁷ we have made a composite table of the data in each group, which illustrates the findings discussed very clearly.

Of our series of 118 patients with cholecystitis with stone formation, 110 were treated by cholecystectomy; of these, 6 died after operation (table 2). The remaining 8 were treated by cholecystostomy, and of these, 3 died. The high mortality (37.5 per cent) after cholecystostomy may be explained by the fact that this type of operation is employed at the Mount Sinai Hospital only on patients whose general condition precludes the employment of any drastic form of surgical intervention.

8. Peterson, T.: Gall Bladder Disease: A Critical Clinical Study, Minnesota Med. 18:123-127 (Feb.) 1935.

Lipshutz,⁹ in a recent study, concluded that the operative mortality in cases of acute cholecystitis is less when operation is performed as soon as the patient has been adequately prepared with dextrose and fluids than when operation is deferred. Mentzer,¹⁰ in a study of 43 cases of acute cholecystitis, found that what appears to be a mild or moderately severe cholecystic inflammation clinically may actually be a fulminant cholecystitis. Mentzer, Kirschner and Nordmann (cited by Bashein¹¹) and many other surgeons advocate early operative intervention, usually cholecystectomy, in cases of acute cholecystitis. The findings in our present study are in accordance with this point of view. Twenty-two patients with acute cholecystitis associated with stones were treated by cholecystectomy, with 1 death, a mortality of 4.5 per cent. Seven patients with acute cholecystitis were treated by cholecystostomy, with 2 deaths, a mortality of 28.5 per cent.

TABLE 1.—*Correlation of Pathologic Changes, Clinical Symptoms and End-Results in 147 Cases of Cholecystitis Without Stones*

Pathologic Lesion Present		Results in Cases With History of Biliary Colic (52)			Results in Cases Without History of Biliary Colic (95)		
		Well	Im-proved	Unim-proved	Well	Im-proved	Unim-proved
Mackey's cases	Minimal lesion.....	2	6	7	9	15	15
	Cholesterosis.....	8	0	5	6	2	11
	Chronic catarrhal cholecystitis....	10	6	1	7	12	13
	Chronic fibrous cholecystitis.....	1	1	0	1	2	0
Authors' cases	Chronic fibrous cholecystitis.....	2	3	0	0	0	2
	Total of both groups.....	23	16	13	23	31	41

The average period of preparation for the patients with acute cholecystitis who were subjected to cholecystectomy ranged from two and four-tenths to three and six-tenths days (table 2). The average period of convalescence of these patients with acute gangrenous calculous cholecystitis and acute exacerbation of a chronic calculous cholecystitis was thirteen and a half days. Three patients with acute ulcerative calculous cholecystitis had an average convalescence of eighteen and three-tenths days. The average period of preoperative hospitalization for the 88 patients with subchronic and chronic cholecystitis was about nine days, as compared with the average of three days for those with acute cholecystitis. This is explained by the fact that many of the

9. Lipshutz, B.: Acute Cholecystitis, *Ann. Surg.* **101**:902-911 (March) 1935.

10. Mentzer, S. H.: Acute Gall Bladder Manifesting Few Signs or Symptoms, *Surg., Gynec. & Obst.* **55**:709-716 (Dec.) 1932.

11. Bashein, H.: Gall Bladder Surgery: Observations from Series of Cases as to Advantages of Early Operations, *Am. J. Surg.* **23**:506-513 (March) 1934.

patients in the first two groups were usually admitted to the medical services for complete study before being subjected to operation.

We were able to obtain follow-up data on 17 of the 29 patients with acute cholecystitis who were operated on. All 17 were either completely cured or else greatly improved. This finding is in sharp contrast to the results obtained by cholecystectomy in cases of non-calculous cholecystitis, as shown in table 1; in a series of 147 patients, 56, or 38 per cent, failed to be relieved or were made worse by the operation.

Of the 88 patients with subchronic or chronic cholecystitis with stone who were treated by cholecystectomy, 6, or 6.8 per cent, died after operation. Of the remaining 82, we were able to obtain follow-up data on 50. In this group 28 regarded themselves as cured, and 21 stated that they were greatly improved, suffering only from occasional attacks of dyspepsia after dietary indiscretions. Only 1 patient in this group was found to be unimproved. Thus, of the group of 104 patients with calculous cholecystitis who survived cholecystectomy, we were able to obtain follow-up data on 63. Of these, 62, or approximately 98 per cent, were either cured or greatly improved, while only 1 patient showed no improvement.

Statistical and follow-up data in the recent literature on cases of disease of the gallbladder¹² are in overwhelming agreement as to the most important criteria for establishing a diagnosis of such a condition.

1. A typical history, which includes intermittent pain in the right upper abdominal quadrant, with or without jaundice, and a persistent gaseous indigestion characterized by a qualitative dyspepsia for fried and fatty foods, is an important indication. According to Stanton,^{12a} if a surgeon is definitely certain of his ground relative to the clinical history of biliary colic, he can proceed to remove the gallbladder even if there is no obvious recognizable pathologic process present at the operative table.

Table 3 shows that colic, which was present in 112 of 118 cases of various types of cholecystitis, is the most constant clinical symptom and substantiates what Stanton has said about the significance of biliary colic. Additional justification for the removal of the gallbladder in these cases may be found in the fact that of the 63 patients on whom a follow-up study was made, 62 were either cured or greatly improved.

12. (a) Stanton, E. M.: Stoneless Gall Bladder: Study of Operative Cases, *Am. J. Surg.* **18**:246-250 (Nov.) 1932. (b) Hitzrot, L. H.: Correlation of Other Diagnostic Procedures with Cholecystography in Two Hundred and Fifty Cases of Suspected Gall Bladder Disease, *Am. J. M. Sc.* **186**:203-213 (Aug.) 1933. Mackey.⁷

TABLE 2.—*Correlation of Pathologic Changes and Clinical Course in 118 Cases of Calculous Cholecystitis*

Pathologic Lesion Present	No. Cases	Duration of Symptoms					Period of Preparation	Average Postoperative Period in Hospital	Results of Follow-Up Study			No. Without Follow-Up Study	
		1 Yr.	1-5 Yr.	5-10 Yr.	Over 10 Yr.				Died	Well	Im- proved		Unim- proved
						Cholecystectomy (110 Cases, with Follow-Up in 62)							
Acute gangrenous cholecystitis.....	13	5	8	0	0	2.4 days after ad- mission (12 cases), 41 days (1 case)	13.6 days	0	4	4	0	5	
Acute ulcerative cholecystitis.....	3	3	0	0	0	3.6 days	18.3 days	0	0	2	0	1	
Acute exacerbation; chronic cholecystitis	6	2	0	0	4	3.5 days	13.0 days	1	2	1	0	2	
Subchronic cholecystitis.....	41	5	15	14	7	9.2 days	15.4 days	2	14	8	0	17	
Chronic cholecystitis.....	47	8	21	7	11	8.7 days	14.2 days	3	13	13	1	17	
Total.....	110	23	44	21	22			—	—	—	—	—	
						Cholecystostomy (8 Cases)		6	33	28	1	42	
Acute ulcerative cholecystitis.....	1	0	1	0	0			1	0	0	0	0	
Acute exacerbation; chronic cholecystitis	6	2	3	1	0	Immediate (3 cases), 10.5 days (4 cases)	26.4 days	1	4	0	0	1	
Chronic cholecystitis.....	1	0	0	0	1			1	0	0	0	0	

2. The cholecystogram is the most important single clinical test in establishing a positive diagnosis of disease of the gallbladder. Rose¹³ summarized the work of 20 authors, reporting a total of 39,280 cases, in 5,983 of which operation was performed, and added 911 cases of his own, in 295 of which operation was performed. He concluded that the roentgenographic diagnosis of a pathologic process of the gallbladder is dependable to the extent of 98 per cent. Ferguson and Palmer,¹⁴ in a review of 2,070 cases extending over a period of five years, arrived at approximately the same conclusions as Rose. However, the roentgenographic diagnosis of a normal gallbladder is correct, on the average, in only about 76 per cent of the cases. This finding may be explained, according to Burden,¹⁵ by his observation that an incompetent sphincter of Oddi will not permit of proper filling of the gallbladder or of concentration of its contents. On the other hand, a spastic sphincter, which

TABLE 3.—*Correlation of Pathologic Changes with Clinical Symptoms and End-Results in 118 Cases of Calculous Cholecystitis*

Pathologic Lesion Present	No. of Cases	Jaundice	Qualitative Dyspepsia	Colic	Well	Improved	Unimproved
Acute gangrenous cholecystitis.....	13	4	3	13	4	4	0
	4	1	0	4	0	2	0
	12	4	5	12	2	1	0
	41	10	19	39	14	8	0
	45	12	17	44	13	13	1
Total.....	118	31	44	112	33	28	1

is frequently present in cases of cholecystitis, will allow and even promote proper filling and concentration in the gallbladder, thus giving rise to a normal cholecystogram even though the gallbladder is diseased.

According to the statistics of Moore,¹⁶ Hauser,² Clute and Swinton¹⁷ and Hitzrot,^{12b} the diagnosis based on the cholecystogram is correct in 90 per cent of the cases and is of equal value whether the dye is given by mouth or intravenously. Persistence of the shadow after a fatty meal is indicative of a pathologic condition of the gallbladder. In

13. Rose, C. B.: Some Problems and Results in Cholecystography, *Radiology* **22**:197-201 (Feb.) 1934.

14. Ferguson, A. N., and Palmer, W. L.: Cholecystography: Its Clinical Evaluation; Study of Two Thousand and Seventy Cases, *J. A. M. A.* **100**:809-812 (March 18) 1933.

15. Burden, V. G.: X-Ray Gall Bladder: Surgical Opinion, *Am. J. Surg.* **22**:60-63 (Oct.) 1933.

16. Moore, S.: Cholecystography: Analysis After Six and One-Half Years' Application, *J. A. M. A.* **95**:1957-1961 (Dec. 27) 1930.

17. Clute, H. M., and Swinton, N. W.: Management of Gallstones: Review of Two Years' Experience, *S. Clin. North America*, **14**:1137-1145 (Oct.) 1934.

comparison with a positive clinical history and a positive cholecystogram, the icterus index, the qualitative and quantitative van den Bergh tests, duodenal drainage and fractional analysis of the gastric contents are only of secondary importance in the diagnostic armamentarium.

A glance at table 4 shows that in our group of 133 patients cholecystographic studies were done on 58. The cholecystographic picture was correct, as far as disease of the gallbladder other than stone is concerned, in 82.7 per cent. The diagnosis as to the presence or absence of stone was made correctly by the cholecystogram in only 51.7 per cent of the patients studied. The latter results may be explained by the fact that about 60 per cent of biliary calculi are radiolucent and are therefore not visualized by the cholecystogram. Flat roentgenograms were made of only 8 patients, with a 50 per cent correct diagnosis for the presence or absence of stone.

TABLE 4.—*Correlation of Cholecystogram and Flat Roentgenogram with the Operative and Pathologic Pictures*

Roentgenographic Picture	Absence of Stone*		Presence of Stone†	
	No.	Pathologic Picture	Chronic Cholecystitis	Acute Cholecystitis
Cholecystogram				
Reported normal	2	Chronic cholecystitis	3	1
Nonfilling or poor filling with stone	2	Chronic cholecystitis without stone	19	1
Nonfilling or poor filling without stone	5	Chronic (4 cases), congested (1 case)	18	3
Normal filling with no shadows	1	Chronic	3	0
Flat roentgenogram				
Evidence of stone	1	Subchronic, no stones	2	2
No evidence of stones	0		3	0

* Roentgenographic studies were made on 11 of 15 patients without stone.

† Roentgenographic studies were made on 55 of 118 patients with stone.

3. Laboratory studies are of some diagnostic importance. In spite of the great amount of work that has been done in studying the functions and chemistry of the liver, investigators are still in the dark when they try to evaluate the state of hepatic function in a particular case. The various dye tests and the galactose tolerance test are of some value in estimating some of the functions of the liver but are insufficient to answer the question as to what will be the physiologic response of the liver in a given case in the event that a laparotomy is performed.

Fowler¹⁸ said that in 80 of 100 patients with disease of the gallbladder the symptoms subside or can be successfully treated medically, but he is contradicted by his own statistics, which cover a study of 979 patients. His figures show that a higher mortality and morbidity and failure to obtain relief from symptoms occur in patients who are treated medically for a long time, in whom pathologic processes

18. Fowler, R. S.: Gall Bladder Disease: One Thousand End Results, *Am. J. Surg.* 22:53-59 (Oct.) 1933.

pursuant to the disease of the gallbladder are allowed to develop. The greatest factor in deaths from disease of the biliary tract appears to be the delayed operation, which permits of the development of the train of physiologic and pathologic changes that occur with the passing of time.¹⁹ It must be remembered that disease of the gallbladder often affects other surrounding organs²⁰ besides the liver, frequently causing chronic pylorospasm, pancreatitis and possibly cardiac²¹ and renal derangement. Lahey has well said "our medical friends must overcome the complacency with which they permit patients to go through repeated attacks of gall-stone colic" (quoted by Palmer^{19a}).

Goldish and Gillespie²² showed that the average age of the patients who have died after operation for disease of the gallbladder is 10.3 years greater than that of those who lived. Heuer²³ concluded that the difficulties which beset the surgeon during and after the operation are the results of prolonged disease. The deeply jaundiced patient with obstruction of the common duct, lowered vitality, poor resistance to infection, renal damage and a tendency to hemorrhage presents an example of the result of prolonged disease; such a patient will die all too frequently notwithstanding the best surgical measures.

Of the 9 patients who died after operation (table 5), 7 were women, ranging in ages from 45 to 64 years; 5 gave a history of symptoms relative to the gallbladder extending over five years and 2 over ten years. Although none of these deaths definitely fall into any of the three groups of "liver deaths" as described by Heyd,²⁴ the liver showed pathologic changes, severe in many instances, in all of the cases in which autopsy was performed. Multiple abscesses of the liver were found in 5 of the 8 patients on whom autopsy was performed, and hepatitis of varying severity was found in 7. All of the 9 with a history of prolonged involvement of the gallbladder showed evidence also of involvement of the pericholecystic structures, the liver, pancreas or kidneys or

19. (a) Palmer, D. W.: Preoperative Pathology in Its Relation to Post-Operative Gallbladder Deaths, *Ohio State M. J.* **30**:293-297 (May) 1934. (b) Pratt, G. H.: Cholecystectomy and Cholecystostomy in Acute Suppurative and Gangrenous Cholecystitis, *Am. J. Surg.* **22**:46-52 (Oct.) 1933. (c) Bashein.¹¹

20. Mason, J. T., and Blackford, J. M.: Conservative Treatment of Cholecystitis, *J. A. M. A.* **99**:891-893 (Sept. 10) 1932.

21. Schwartz, M., and Herman, A.: Association of Cholecystitis with Cardiac Affections: Study Based on One Hundred and Nine Cases, *Ann. Int. Med.* **4**:783-794 (Jan.) 1931.

22. Goldish, D. R., and Gillespie, M. G.: Review of Three Hundred and Forty-Seven Gall Bladder Operations, *Am. J. Surg.* **21**:30-37 (July) 1933.

23. Heuer, G. J.: Factors Leading to Death in Operations upon Gall Bladder and Bile Ducts, *Ann. Surg.* **99**:881-892 (June) 1934.

24. Heyd, C. G.: Liver Deaths in Surgery of Gallbladder, *J. A. M. A.* **97**:1847-1848 (Dec. 19) 1931.

TABLE 5.—Analysis of Cases of Cholecystitis in Which Death Occurred After Cholecystectomy and Cholecystostomy

Case No.	Patient	Age	Sex	Duration and Symptoms	Period Covered by Past History	Operation	Operative Findings	Clinical Course	Time of Death After Operation	Necropsy
1	A.B.	46	F	5 days; jaundice; colic	6 yr.	Cholecystostomy	Acute ulcerative calculous cholecystitis; stone in cystic duct; abscess of gallbladder bed	Paralytic ileus	3 days	Acute ulcerative cholecystitis; abscesses of liver; localized peritonitis; fatty infiltration of pancreas
2	M.D.	64	F	1 mo.; colic and dyspepsia	12 yr.	Cholecystostomy	Shrunken gallbladder; many stones; stone in cystic duct; hepatitis; adhesions	Septicemia; positive blood culture	4 days	Chronic cholecystitis; abscesses of liver; localized peritonitis; periportal cirrhosis
3	R.S.	55	F	3 wk.; jaundice; colic; dyspepsia	12 yr.	Cholecystectomy; choledochotomy	Gangrenous cholecystitis; stone in common bile duct; adhesions	Severe postoperative shock; hematemesis	5 days	Subchronic exacerbation of focal necrosis; abscesses of liver; infarction of liver; portal cirrhosis
4	A.G.	40	M	10 days; chills; fever; jaundice	6 yr.	Cholecystectomy; appendectomy	Chronic calculous cholecystitis; appendical abscess	Chills, fever and intestinal obstruction	47 days	Suppurative pyelophlebitis of portal vein; abscesses of liver; gangrene of small intestines
5	E.B.	46	F	2 wk.; qualitative dyspepsia	7 yr.	Cholecystectomy	Chronic cholecystitis; adhesions	Intestinal obstruction due to adhesions	3 days	Chronic cholecystitis; adhesions producing obstruction; postoperative shock; fatty infiltration of liver and pancreas
6	P.B.	48	F	4 days; vomiting; fever; uremia	5 yr.	Cholecystectomy	Chronic calculous cholecystitis	Abdominal distention; pulmonary atelectasis	13 days	Multiple hemorrhagic areas; necrosis and hepatitis; purulent bronchitis
7	B.M.	45	F	2 mo.; chills; fever; jaundice; colic	5 yr.	Cholecystectomy; choledochotomy	Chronic calculous cholecystitis; pericholecystic adhesions; induration of liver and pancreas	Hematemesis; melena; hemorrhage from operative site	20 days	Secondary hemorrhage from operative site; diffuse hepatitis; abscesses of kidneys
8	A.J.	60	F	3 mo.; colic; qualitative dyspepsia	10 yr.	Cholecystectomy	Acute exacerbation; chronic calculous cholecystitis; pericholecystic adhesions	Circulatory collapse; laparotomy showed no hemorrhage	1 day	No necropsy
9	J.F.	35	M	1 day; fever; colic	0	Cholecystostomy	Acute gangrenous calculous cholecystitis	Abdominal distention; anuria; uremia on third day after operation	7 days	Uremia; gangrenous cholecystitis; local peritonitis; adhesions; portal cirrhosis; fatty infiltration of pancreas; congenital aplasia of right kidney; toxic nephrosis

combinations of these organs. The presence of adhesions in 6 of these patients made operation more difficult. In case 5 the many adhesions present caused intestinal obstruction and finally death. The patient in case 2 died of septicemia, which undoubtedly was present but unrecognized prior to operation. A blood culture taken on the day after the operation was positive for Friedländer's bacillus. Case 4 should not really be listed under "gallbladder death," although the history pointed to disease of the biliary tract. Operation in this case revealed besides chronic calculous cholecystitis, an appendical abscess in which the appendix had sloughed off. Suppurative pyelophlebitis with multiple abscesses of the liver and infarction and gangrene of several feet of small intestine developed, and the patient died. In case 9 anuria developed within twenty-four hours postoperatively, and the patient died six days later of uremia. This case might be regarded as an example of the "hepatorenal" syndrome described by Schutz and his co-workers.²⁵

COMMENT AND SUMMARY

We have presented a clinical and pathologic review of disease of the gallbladder in 133 patients who were operated on at the Mount Sinai Hospital from 1930 to 1935. Of this group, we have been able to obtain informative follow-up data on 83 persons. Although our group is too small to permit drawing definite conclusions regarding any single phase of disease of the gallbladder and its treatment, nevertheless, we feel that we are justified in stressing the following observations:

1. The clinical history of biliary colic, and to a lesser extent of qualitative dyspepsia for fried and fatty foods and of jaundice, is of primary importance in the establishment of a diagnosis of disease of the biliary tract. Of the clinical tests, the cholecystographic study is the most important, and in our series of 58 cases a correct diagnosis was made in 82.7 per cent.

2. The results of cholecystectomy on patients with noncalculous cholecystitis were better when the patient presented a definite history of biliary colic and a definite pathologic process was found at operation. Cholecystectomy on patients with noncalculous cholecystitis in whom the pathologic process was minimal and the clinical history of biliary colic was not definite resulted in relief of symptoms in only about 56 per cent as compared to cure or great improvement in 67 per cent of those giving a definite history of biliary colic.

3. Our follow-up data on 63 patients with calculous cholecystitis showed that the clinical results are far better in those with stone than

25. Schutz, C. B.; Helwig, F. C., and Kuhn, H. P.: Contribution to Study of So-Called Liver Deaths, *J. A. M. A.* 99:633-636 (Aug. 20) 1932.

in those without stone. Of the 63 patients about whom information was obtained, 62 were either cured or greatly improved, a percentage of 98.4 as compared to the 63.2 per cent of the noncalculous group.

4. The results following cholecystectomy on 22 patients with acute cholecystitis included in our group with calculous cholecystitis indicate that a radical operation as soon as the patient has been adequately prepared is the desirable mode of treatment. Of the 22 patients presenting acute gangrenous, acute ulcerative or an acute exacerbation of chronic cholecystitis, only 1 died after operation. Both the morbidity and the mortality in the cases of acute cholecystitis were less after cholecystectomy than after cholecystostomy.

5. Our review of disease of the biliary tract in 133 patients has shown that there is a direct relationship between the duration and the severity of the clinical symptoms, the morbidity and mortality and the character of the pathologic lesions noted at operation and at necropsy. The significant part which the pericholecystic complications, the result of prolonged medical treatment for disease of the gallbladder, played in the fatal outcome of the 9 patients justifies a plea for early operative treatment of patients suffering with disease of the biliary tract after a definite diagnosis has once been established.

Drs. B. Lipshutz, M. Behrend and E. L. Eliason granted permission for the inclusion of their cases in this report.

CARCINOMA OF THE SUPRAPAPILLARY PORTION OF THE DUODENUM

HAROLD L. STEWART, M.D.

BOSTON

AND

MARSHALL M. LIEBER, M.D.

PHILADELPHIA

The purpose of this communication is to report six cases of carcinoma of the suprapapillary segment of the duodenum and to analyze and summarize the data obtained from the reported cases of this condition. Reports of one hundred and four cases were abstracted from the literature, thirty-five¹ of which were regarded as acceptable on the basis of the data presented, a clinical history and gross and microscopic studies of the primary lesion being presented in each report. Twelve² additional cases, although probably authentic examples of this condition, could not be included in the present analysis because of insufficient clinical or pathologic data. Fifty-seven more reported cases were discarded, nineteen because, owing to involvement of the stomach, pancreas or bile passages in the malignant process,³ the duodenal origin of the lesion was not established with certainty and thirty-eight⁴ because the histologic

From the Pathological Laboratories of the Jefferson Medical College and Hospital, the Jefferson Hospital Tumor Clinic and the Philadelphia General Hospital.

1. Coupland; Ewald; Montgomery and Sherman; Pic (case 1); Letulle; Aaron; Gerster; Geiser (case 1); Bibby and Stewart; Jefferson; McGuire and Cornish (case 3); Herman and von Glahn; Ramond, Vincent and Clémont (case 1); Van Tienhoven (case 2); Morrison and Feldman; Dewis and Morse (cases 1, 2, 3, 4 and 5); Kettle; Archibald; Pacetto; Lageder; Meyer and Rosenberg (case 2); Mateer and Hartman (case 1); Rutishauser (cases 1 and 5); Cave (cases 8 and 11); Eger (case 1); Lisa; Levine and Fitzhugh (case 2); Dardinski; Ochsner and Wilbur (case 2); von Hrabovsky (case 2); Doub and Jones (case 1—the same as reported by Mateer and Hartman, case 1); McNamara, and Bastos.

2. Geiser (case 4); Peck; Reichel and Staemmler (cases 2 and 3); Borrmann (cases 1 and 2); Arisz (cases 1 and 2); Raiford (cases 46597 and G 662); Bookman; Schüssler (case 1) and Rutishauser (case 4).

3. Fullet; Drechsler; Bérangier; Coupland; Höft; Trémolières; Geiser (case 9); Benedict; Bassler and Grant; Lichty (cases 1 and 3); Judd (case 2); Orator (cases 1 and 2); Cabot (case 15111); Hinton (cases 1 and 3); Popovici, and Wilson and Noble.

4. Haley; Carrer; Dickinson; Cayla; Boyé; Whittier (case 12); Pye-Smith; Weecke; Perry and Shaw; Pic (case 2); Günther; Czygan; Heynen; Wurm

(Footnote continued on next page)

studies were not reported, the diagnosis apparently having been made on the basis of gross examination alone. Of historical interest are the cases reported by Hamberger (1746) and Morgagni (1761).

REPORT OF CASES

CASE 1.—J. P., a white man aged 35, whose complaints were belching, vomiting, anorexia and a loss of 30 pounds (13.6 Kg.) in weight, was admitted to the Jefferson Hospital on March 22, 1931, with the clinical diagnosis of carcinoma of the head of the pancreas. For years he had been troubled with gas and belching. In November 1929 he experienced a brief attack of severe epigastric pain, which was followed a week later by jaundice. At operation on Jan. 2, 1930, in another hospital, a markedly thickened gallbladder containing many stones was removed, together with several drachms of gravel from the common bile duct, which was incised and drained. Jaundice did not entirely disappear owing to obstruction at the ampulla of Vater, and the drainage tube could not be removed from the common duct. A choledochogastrostomy stoma was then established, and the jaundice cleared entirely, the patient remaining practically free from symptoms until February 1931. Again jaundice recurred, associated with vomiting, excessive gas and pain in the right upper abdominal quadrant, and the patient was admitted to the Jefferson Hospital on March 22.

Physical examination revealed tenderness in the right upper abdominal quadrant and a palpable mass, which descended with inspiration. The hemoglobin content of the blood was 27 per cent, the red cell count 1,280,000, the white cell count 1,100 and the color index 1.01. There were polychromasia and stippling, with many microcytes, macrocytes and poikilocytes. The urine was alkaline, contained albumin and had a high specific gravity varying from 1.016 to 1.030. The stools contained blood and an excessive amount of fat. There were blood and bile in the vomitus, which showed a free acidity of 18 and a total acidity of 28. A roentgenogram of the gastro-intestinal tract was unsatisfactory because of considerable retention of food. With treatment the hemoglobin content increased to 43 per cent, the red cells to 2,850,000 and the white cells to 8,200. At laparotomy on April 14, local anesthesia being used, the stomach appeared pale and distended and the jejunum pale and collapsed. On account of dense adhesions it was not possible to make a satisfactory examination of the duodenum and bile ducts. A large, irregular, firm, slightly tender mass, 7.7 cm. in diameter, was palpated in the retroperitoneal region, and a posterior gastro-enterostomy was performed in the usual manner. That night there was slight oozing of blood from the wound, the patient was markedly dehydrated, the chloride content of the blood was 406.9 and the carbon dioxide-combining power rose from 98 to 128. Fluids were administered subcutaneously and intravenously, and a small transfusion of blood was given. The following evening the pulse became rapid and the temperature high, and there was a marked drop in the blood pressure. The patient died from hemorrhage on March 17.

Autopsy was performed four hours after death. The combined gross anatomic and microscopic diagnoses were: (1) annular constricting adenocarcinoma of the

(cases 1 and 2); Friedrich (cases 1 and 2); Moynihan (cases 1 and 2); George and Leonard; Helm; Judd (cases 1, 3, 4 and 5); McGuire and Cornish (case 4); Vervloet; Eusterman; Berkman and Swan (cases 1, 2, 3, 4, 5 and 6); Brüning; Dewis and Morse (cases 8 and B); Hanganutz, and Brdiczka.

suprapapillary portion of the duodenum with constriction of the common bile duct and extension and metastases to the pancreas, regional lymph nodes and surrounding tissues; (2) hydrohepatosis with marked jaundice; (3) chronic interstitial pancreatitis; (4) recent gastro-enterostomy; (5) peritoneal, pericardial and bilateral pleural effusions, and (6) pulmonary edema and congestion.

Dense fibrous adhesions passed between the fossa of the gallbladder and the lower end of the stomach and duodenum, including the inferior margin of the liver, which was adherent to the anterior abdominal wall. The lumen of the duodenum just proximal to the ampulla was practically completely obliterated by an annular constricting lesion. The mucous membrane in this area appeared thickened and nodular but apparently was not ulcerated. There was marked neoplastic induration of the wall of the duodenum, with direct extension into the pancreas and the surrounding tissue.

The proximal portion of the duodenum and stomach were greatly distended, and the pyloric ring was completely effaced. The lower border of the stomach extended below the umbilicus; its mucosa was atrophic, and its lumen contained bile-stained, bloody fluid. The margins of the gastro-enterostomy opening were intact but swollen and edematous. A choledochogastrostomy opening did not exist, and there was no gallbladder. The lower end of the common bile duct was buried in a mass of adhesions and cancer tissue. A probe was passed with difficulty through the ampulla of Vater into the common bile duct, which was markedly thickened and dilated. The liver was irregular on the surface, and the capsule was thickened and covered with dense adhesions, especially on the under-surface. On section the hepatic tissue was dark greenish brown, the normal markings were absent, there was a good deal of fine fibrosis and the intrahepatic ducts were markedly thickened. Many of the mesenteric, peripancreatic, retro-peritoneal and periaortic lymph nodes were enlarged, firm and gray, measuring from 2 to 3 cm. in diameter.

Sections from the constricting lesion in the duodenum showed the mucous membrane to be markedly thickened (fig. 1) and interspersed with large areas of atypical epithelium. Brunner's glands formed a thick, practically continuous submucosal layer. Malignant transformation appeared to occur first in the deeper parts of the mucosa, where the cells became irregular in shape, often rounded, and were closely packed instead of forming crypts. For a space they seemed to respect the muscularis mucosa, penetrating it only in limited small areas. These cells permeated through Brunner's glands (fig. 2), tending to follow the supporting stroma, and on reaching the submucosal areolar tissue spread out laterally almost the entire length of the sections. They infiltrated in and between the muscle bundles, usually at right angles to the length of the section, and were seen deep to the muscle (fig. 3). One large nerve was invaded, and epithelial cells were seen in small veins, arteries and lymphatics. In places the cells formed small acini of cuboidal or columnar cells, but elsewhere there was no characteristic arrangement, the cells being in dense clumps or in slender strands separated by fibrous tissue. The individual cells were variable in size and shape but usually small, with round and ovoid hyperchromatic nuclei, which were sometimes marginal and crescent shaped, giving the cell a signet ring appearance. No mitotic figures were seen. The fibrous stroma was scant in the mucosa but more abundant deep in the wall of the duodenum.

There were marked atrophy and fibrosis of the pancreas within and about the lobules. Lymphocytes were scattered throughout and tended to clump about the ducts, nerves and infiltrating strands of atypical epithelial cells. The tumor

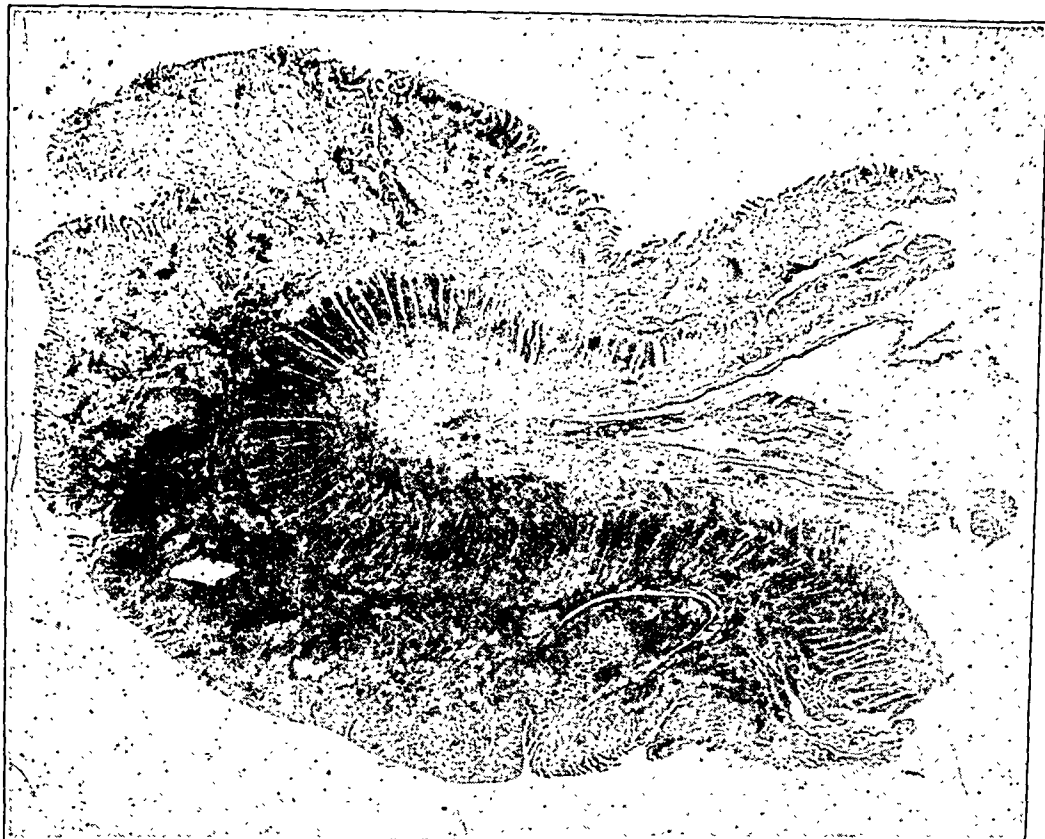


Fig. 1 (case 1).—Section from the constricting lesion in the duodenum, showing marked neoplastic thickening of the mucous membrane; circa $\times 7$.

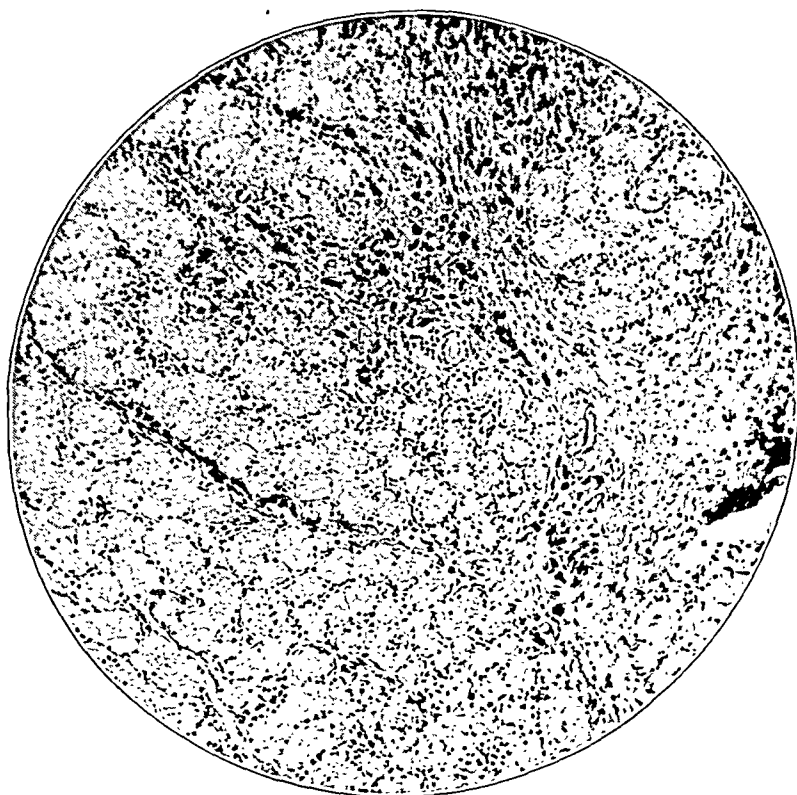


Fig. 2 (case 1).—Section of the duodenal lesion showing neoplastic permeation of Brunner's glands: $\times 100$.

tissue here had a more abundant stroma than in the intestine and was frequently observed surrounding nerves and vessels.

Sections of a lymph node showed almost complete replacement by a dense mass of undifferentiated epithelial cells with little stroma, the atypical appearance of the cells being a striking feature.

The liver presented the characteristic picture of biliary stasis, with granules and droplets of bile pigment, bile casts and degeneration and necrosis in the inner third of the lobule. The sinusoids were dilated, the small bile ducts were proliferated and there was a marked increase in periportal connective tissue, which frequently completely encapsulated the lobules. Scattered throughout the sections



Fig. 3 (case 1).—Section of the duodenum showing a small strip of mucous membrane, Brunner's glands and the underlying muscle. The neoplastic cells have permeated the connective tissue stroma of Brunner's glands and have infiltrated in and between the muscle bundles frequently at right angles to the length of the section; $\times 50$.

were numerous focal midzonal and biliary necroses, which were often converted into small abscesses.

CASE 2.—C. N., a white man aged 69, whose complaints were vomiting, constipation, abdominal distress and marked thirst of two weeks' duration, was admitted to the hospital on Jan. 30, 1924, with the clinical diagnosis of carcinoma of the pancreas. During the preceding half year he lost 15 pounds (6.8 Kg.) in weight. The onset of the terminal illness occurred suddenly one evening on Jan. 13, 1923, with the vomiting of a large quantity of light frothy material, unassociated with pain or nausea. The patient returned to work the following

day but vomited that night after the evening meal and on each succeeding night for a week. At first the vomiting was not forceful, but later he had to support his abdomen because of retching. There were tarry stools, slight constipation, a good deal of belching with the attacks of vomiting and frequent eructations of sour fluid. On physical examination the epigastric region was distended and slightly rigid but not tender, and no definite mass was visible or palpable. There were a marked grade of secondary anemia and a leukocytosis of 22,600. The urine had a specific gravity of from 1.017 to 1.025 and contained albumin and casts. The stools contained blood. The gastric content showed a residual total acidity of 34 and free hydrochloric acid of 19; after a test meal these figures gradually rose to a maximum of 49 and 30, respectively, at the end of two hours. Four days after admission the patient fainted after vomiting 100 cc. of thick dark brown material. He regained consciousness after a short interval but was weak, cold and restless and complained of severe pain in the lower part of the abdomen. That night he vomited 250 cc. of bright red blood and died five minutes later.

Autopsy was performed thirteen hours after death. The combined gross anatomic and microscopic diagnoses were: (1) adenocarcinoma of the suprapapillary segment of the duodenum, with extension to the pancreas and metastasis to the liver and peritoneum; (2) duodenal hemorrhage; (3) hemoperitoneum; (4) pulmonary emphysema, congestion and edema; (5) arteriosclerosis of the aorta and renal arteries; (6) chronic nephritis, and (7) fibrosis and degeneration of the myocardium.

In the duodenum just distal to the pylorus was a soft dark reddish green ulcer, 3 by 5 cm., which completely encircled the intestine. The wall of the duodenum was composed of firm gray tissue, which extended laterally in the muscular coat beneath the pyloric ring into the wall of the stomach for 2 cm. The duodenum at the site of the ulcer was bound to the head of the pancreas, which was infiltrated by a tumor mass, 1.5 cm. in diameter, continuous with the lesion in the duodenum. The distal aspect of the duodenal lesion was sharply limited by normal mucosa. The stomach and esophagus were distended with blood. The peritoneum contained several firm gray nodules, measuring from 1 to 3 mm. in diameter, on the under-surface of the diaphragm and in the visceral serosa of the small and large intestine.

The liver weighed 2,080 Gm. and was reddish brown and soft. There were many circumscribed firm gray nodules, averaging 2 cm. in diameter, which formed a large confluent mass in the edge of the right lobe. The largest of these nodules showed necrotic centers, while those on the surface were regularly umbilicated. The biliary passages were patent.

There were bilateral congestion and edema of the lungs and several small, firm, discrete, pearly gray subpleural nodules.

Histologic sections of the duodenal lesion disclosed a transition from normal mucous membrane into a large area of atypical epithelial cells showing extensive necrosis and hemorrhage. Lateral to the area of ulceration Brunner's glands were hyperplastic, but immediately underneath it they were destroyed by the cancer tissue, which permeated the stroma of these structures. The tumor cells penetrated through all coats of the intestine and spread out laterally into the surrounding fat along the peritoneal surface. The cells were discretely arranged, large, round or oval elements with acidophilic or basophilic vacuolated cytoplasm and relatively small oval or sickle-shaped hyperchromatic nuclei, which were often eccentrically situated. Other nuclei were large and pale with multiple lobulations and occupied

a more central position in the cell. Mitotic figures were rare. A large amount of stringy mucinous material was present between the cells and in the cytoplasmic vacuoles. The tumor cells were further separated into nests and linear masses by strands of avascular connective tissue infiltrated with small round cells. In the depths of the main tumor a few acini lined with cuboidal and columnar cells were observed, and many large blood vessels contained tumor cells.

The large tumor nodules in the liver showed extensive hemorrhage and necrosis. The atypical epithelial cells grew in solid nests in some places, but mainly they were desquamated into small alveolar spaces enmeshed in stringy mucinous material. As a rule the cells had an abundance of finely vacuolated cytoplasm, which contained droplets of mucin. Many nuclei were oval and eccentrically placed in the cell, while others were large, irregular and hyperchromatic. The stroma was abundant and hyalinized.

In the under-surface of the diaphragm the tumor cells formed nests and acini supported by dense connective tissue stroma, and there was little tendency to extend below the serosal surface.

CASE 3.—M. C., a physician aged 58, a morphine addict, was admitted to the hospital in a moribund condition on April 15, 1916. A few days previously he had been picked up unconscious from the floor of his home and put to bed by an attendant, who reported that the patient had subsequently passed large quantities of blood by bowel. Because of his stupor and delirium it was difficult to make a satisfactory physical examination during the period of hospitalization, and the findings contained in the clinical record were of little significance with regard to the lesions disclosed at autopsy. It was observed that the patient passed blood by bowel several times. The urine was acid, contained hyaline casts and had a specific gravity of 1.016. The hemoglobin content was 29 per cent, the red cell count 1,880,000, the white cell count 11,600 and the color index 0.8. The patient died two days after admission without regaining consciousness.

Autopsy was performed thirteen hours after death. The combined gross anatomic and microscopic diagnoses were: (1) papillary scirrhus adenocarcinoma of the first portion of the duodenum, with metastasis to the liver and peritoneum; (2) hemorrhage into the intestinal tract; (3) calculous cholecystitis; (4) sclerosis of the aortic and mitral valves; (5) arteriosclerosis of the aorta; (6) acute degeneration of the myocardium and kidneys; (7) cerebral and pulmonary edema, and (8) a small hemorrhagic peritoneal effusion.

An annular ulcer, 5 cm. in diameter, was found in the first portion of the duodenum immediately adjacent to the pyloric sphincter. The edges were hard, indurated and sharply outlined, while the floor was irregular and nodular and contained a small thrombosed vessel. The wall of the duodenum opposite the ulcer was adherent to the neck of the gallbladder. The stomach was markedly dilated, while the remainder of the bowel was dilated and filled with black material.

The peritoneal cavity contained a small amount of blood-tinged fluid. The serosa was smooth, moist and glistening, except for a few small irregular neoplastic nodules on the under-surface of the diaphragm and the right pelvic wall.

The liver was large, soft and pale and contained many firm gray nodules, measuring from 1 to 4 cm. in diameter. The gallbladder was adherent to the wall of the duodenum and the lumen contained 25 cc. of viscid yellow bile and three small faceted calculi.

Microscopic sections of the duodenum disclosed a transition from normal mucosa to an ulcerated neoplastic lesion infiltrating laterally along the submucosa and extending deeply through the muscular wall to invade the peritoneum and

superficial fatty tissue. The tumor cells were usually cuboidal or columnar, but many showed marked variation in size and staining with from one to several hyperchromatic nuclei. A few were observed in mitosis. The cells grew in small nests of imperfect strands but tended generally to reduplicate simple or papillary acinous structures and showed necrosis in many areas. The stroma was abundant, consisting of compact strands of collagenous fibers with a few young and old fibroblasts but not many blood vessels. There was a marked inflammatory reaction consisting of lymphocytes, chiefly limited to the muscular coats along the line of penetration of the tumor cells.

In the liver the atypical epithelial cells appeared to grow along the sinusoids and within the spaces remaining after absorption of necrotic hepatic cells.

CASE 4.—A. W., a white woman aged 85, was admitted to the Philadelphia General Hospital on March 29, 1929, with the clinical diagnosis of chronic intestinal obstruction. According to the clinical record, she had a stroke of apoplexy five years previously followed by impairment of the mental faculties. The terminal illness apparently began in January 1929, with black feces, vomiting and anal pain, both the vomitus and the feces being black. About the middle of March she became bedfast and refused all food; the vomiting continued, and there were no bowel movements until she entered the hospital two weeks later. On physical examination no noteworthy findings were recorded except that the tissues were dehydrated and râles were heard over the thorax. Death occurred suddenly on March 30.

Autopsy was performed twelve hours after death. The combined gross anatomic and microscopic diagnoses were: (1) obstructing primary scirrhus adenocarcinoma of the suprapapillary portion of the duodenum with extension and metastases to the pancreas, the liver and the wall of the gallbladder; (2) calculous cholecystitis; (3) chronic pancreatitis with fatty infiltration; (4) arteriosclerosis of the aorta and the coronary and renal arteries with chronic nephritis, and (5) pulmonary congestion.

The lumen of the duodenum 5 cm. distal to the pylorus was narrowed by a round elevated, indurated ulcer, 2 cm. in diameter. The entire intestinal wall immediately subjacent was firm, indurated, grayish white and adherent both to the pancreas and to the gallbladder. There were no appearances suggesting pancreatic invasion. The gallbladder was contracted about several small faceted greenish yellow concretions together with a small amount of dark grumous bile. On the peritoneal surface near the fundus were two or three small round, grayish white nodules. Its wall was considerably thickened, especially in the region of the neck, which was involved by masses of tumor tissue in the duodenum and liver. The liver weighed 1,120 Gm.; it was firm, and its capsule was thickened; a few grayish white nodules with central yellowish necrotic areas were scattered through the parenchyma. The quadrate lobe was practically entirely replaced by tumor tissue and was densely adherent to the immediately contiguous upper portion of the gallbladder. It was not possible to determine at autopsy whether the tumor arose primarily in the gallbladder, liver or duodenum, but the probabilities were stated in that order, the duodenum being considered the least likely primary site.

The stomach was markedly dilated, and its outline resembled the curve of a fish-hook with the lower border almost at the symphysis pubis. The walls of the stomach were hypertrophied, and the rugae were absent. The body tissues were not jaundiced, and there was no evident obstruction of the biliary passages.

Microscopic sections of the duodenum showed a pale-staining, partially autolyzed mucous membrane, which merged abruptly with an ulcerated area covered with

atypical epithelial cells. The area of ulceration remained comparatively superficial and did not extend below the deep portion of the submucosa. All the coats of the duodenum, however, were involved by cancer tissue. Brunner's glands were completely absent from the area of ulceration but showed no abnormalities in the adjacent portion. The atypical epithelial cells penetrated through all coats of the duodenum and were distributed singly, in small clumps and nests, only rarely reduplicating acinous structures. The cells showed an extreme degree of irregularity in size, shape, staining and number of nuclei; most of them were polyhedral and spindle shaped, with relatively large nuclei and scanty acidophilic cytoplasm, which was usually granular and occasionally contained vacuoles. The cells lining the acinous structures were often cuboidal or columnar. Most of the nuclei were oval or indented and generally enlarged; many were distorted and hyperchromatic, while the largest ones were frequently lobulated, and a few contained inclusions. Only a few mitotic figures were observed. In the musculature tumor cells were observed in small spaces in nerves, and the walls of blood vessels and occasionally in their lumens.

The pancreas showed interstitial fibrosis, fatty infiltration and considerable autolysis. A small area of infiltrating neoplastic cells was noted in one of the large connective tissue septums.

In the liver, in contrast to the duodenum, the tumor cells were more regular, more frequently in mitosis, tended generally to reduplicate acinous structures and showed less supporting stroma. Several of the larger areas of tumor tissue contained central areas of necrosis.

The mucosa of the gallbladder was autolyzed, although the structural outlines of its stroma were well preserved and showed no involvement by tumor tissue. The wall in general and the peritoneal coat especially were markedly thickened, fibrotic and infiltrated with small round cells. The outer portion of the wall was invaded by small clumps of atypical epithelial cells, which stopped short of penetrating through to the mucous membrane.

Nothing was observed microscopically to suggest a cholecystic origin of the tumor. The contracted, thickened and fibrotic character of the gallbladder, together with the presence of biliary calculi and the contiguous relationship the gallbladder bore to the neoplastic lesions in the liver and duodenum, could readily suggest such an origin. A careful evaluation of the anatomic and histologic data warrants the conclusion, we believe, that the lesion under consideration was duodenal in origin. The tumor masses in the gallbladder can be accounted for by extension and metastasis, probably by way of local adhesions, the result of preexisting calculous cholecystitis.

CASE 5.—I. T., an emaciated white woman aged 66, was admitted to the Philadelphia General Hospital on Oct. 21, 1923, with vomiting, loss of weight and weakness. There was a history of an operation for gallstones eight years previously and shortly after that one for "abscess of the stomach." Late in 1922 the patient began to complain of nausea, loss of weight and strength and a feeling of heaviness in the abdomen. In August of the next year frank epigastric pain developed, and the patient vomited constantly. There was no relationship between the taking of food and the onset of epigastric pain, and no blood was detected in the vomitus. On physical examination several nodules believed to lie in the deep fascia were felt in the abdominal wall, which was thin and doughy in consistency. The other resistant masses were palpated in the region of the stomach, the largest of these being 5 cm. in diameter. The patient's course in the hospital was characterized by restlessness, persistent vomiting and progressive weakness and stupor; death occurred on October 24.

Autopsy was performed twelve hours after death. The combined gross anatomic and microscopic diagnoses were: (1) papillary adenocarcinoma of the first portion of the duodenum with metastases to the liver and lungs and the mesenteric and peribronchial lymph nodes; (2) chronic interstitial pancreatitis; (3) arteriosclerosis of the renal arteries with chronic nephritis; (4) chronic adhesive pleuritis and pericarditis; (5) pulmonary edema, and (6) chronic interstitial myocarditis.



Fig. 4 (case 5).—Section of the duodenum showing hyperplastic changes in the muocus membrane and neoplastic involvement of all coats of the intestine; circa $\times 7$.

The duodenum contained a small firm ulcer which measured 2 cm. in diameter and was located 5 cm. from the pylorus and 1 cm. proximal to the papilla of Vater. The margins of this lesion were elevated, indurated and thrown into folds over the central crater-like ulcer. Proximally the stomach and duodenum were dilated, and the wall of the latter was hypertrophied. The regional lymph nodes were enlarged and, with the head of the pancreas, were densely adherent to the wall of the duodenum opposite the primary lesion.

The liver was enlarged in its left lobe and contained many firm white, opaque nodules, measuring from 1 to 5 cm. in diameter. The gallbladder was absent, and the bile ducts were patulous.

Microscopic sections of the duodenum showed a transition from normal mucosa into a zone of hyperplastic and ultimately atypical epithelial cells with a papillary acinous arrangement (figs. 4 and 5). These cells penetrated all coats of the duodenum, including the serosa, which was thick and fibrotic. Brunner's glands were not very numerous and in several places were partially destroyed by invading tumor cells. The malignant transformation appeared to occur first in the superficial cells of the surface mucosa and gradually extended to



Fig. 5 (case 5).—Section of the duodenum showing a transition from normal mucosa into a zone of hyperplastic atypical epithelial cells with a papillary acinous arrangement. The tumor cells penetrate deeply into the submucosa and muscular coat; $\times 40$.

involve the entire thickness of the mucous membrane, the crypts of the glands being involved last. The connective tissue stroma of the mucous membrane near the point of transition was thickened by infiltrating lymphocytes and plasma cells. Some glands were abnormally short, and others were dilated, long and tortuous. The acinous structures were coarse and irregular, with numerous large branches and ramifying cavities lined by from one to several layers of atypical epithelial cells. The lumens of these cystic structures varied in caliber; some contained papillary spurs which grew out perpendicular to the wall, while others were filled with viable or necrotic tumor cells or acidophilic detritus. The majority of the cells were tall columnar elements with rectangular nuclei, while others were

cuboidal or flattened, and a few were greatly enlarged and polyhedral. The nuclei were pale and vesicular and usually situated near the base of the cell. A few were large, irregular and lobulated. Mitotic figures were present but not numerous. The cytoplasm of the atypical cells was abundant, deeply acidophilic and frequently contained single large vacuoles but little if any mucin. Extensive areas of necrosis were present throughout the tumor tissue. The stroma was loose, comparatively scanty and not very vascular. It was infiltrated with clumps of small round cells and leukocytes on the surface of the lesion and around the necrotic areas.

In the liver the tumor nodules were more solid and cellular, with less stroma and inconspicuous acinous and papillary formation.

CASE 6.—E. H., a white man aged 44, entered the Philadelphia General Hospital on April 5, 1913, with gastric pain and jaundice. Pain began eight months previously, coming on after meals in association with belching, but later it assumed a hot burning character and became continuous. The patient was generally constipated and occasionally noticed gross evidence of blood in the stools. Jaundice developed several weeks before admission, but vomiting was never a symptom.

On physical examination jaundice was marked and emaciation extreme. There was fulness of the right upper quadrant, but the remainder of the abdomen was flat. The liver was felt 4.5 cm. below the costal margin, and the left lobe contained a few palpable nodules. Beneath the liver was a tense pear-shaped tumor mass, which moved with respiration.

The patient's course in the hospital was progressively downward. He began vomiting every day at first and finally almost hourly. The vomitus contained large quantities of fresh and of digested blood. An interesting observation was made at the end of the first week, when it was noted that the yellow color of the skin had lightened perceptibly and the gallbladder was barely palpable. The following day, however, the gallbladder became as large as it was formerly.

The urine was acid, had a specific gravity of 1.018 and contained bile. The red cell count was 2,600,000, the hemoglobin content 35 per cent and the leukocyte count 17,000. Blood was present in the feces. The vomitus was green and contained blood and hydrochloric acid. Death occurred on April 21.

Autopsy was performed forty-six hours after death. The combined gross anatomic and microscopic diagnoses were: (1) adenocarcinoma of the suprapapillary portion of the duodenum with extension to the pancreas and metastasis to the liver; (2) hydrohepatosis with marked jaundice; (3) chronic interstitial pancreatitis with extreme atrophy; (4) dilatation of the stomach; (5) hemorrhage into the stomach and intestines; (6) slight myocardial fibrosis; (7) congestion and edema of the lungs; (8) pulmonary anthracosis and emphysema, and (9) arteriosclerosis of the kidney with chronic nephritis and parenchymatous degeneration.

The first part of the duodenum was the seat of an extensive area of ulceration with ragged edges, about 5 cm. in diameter. Directly beneath this lesion was a firm white mass the size of a fist, involving the wall of the duodenum and the head of the pancreas. The remainder of the pancreas was small, white and firm, and the usual lobular appearance was indistinct. The stomach was greatly dilated and contained coffee-ground material. The intestines were distended with gas and bright red blood.

The liver measured 27 by 19 by 8 cm. and extended 3 fingerbreadths below the ribs. It was dark, olive green, tough and resistant to incision. A number of firm white nodules, measuring up to 3 cm. in diameter, were scattered through

the parenchyma. On the surface the centers of these lesions were slightly depressed. The gallbladder was distended with thick bile, little of which could be expressed through the ampulla of Vater.

Microscopic sections of the duodenum showed all the coats infiltrated with masses of irregular tubules composed of a columnar type of cell lying in a framework of adult connective tissue. The stroma was abundant and infiltrated with round cells and polymorphonuclear leukocytes, especially in areas in which the tumor cells were necrotic. A few mitotic figures were observed.

ETIOLOGY

There is a considerable literature devoted to a discussion of the origin of carcinoma of the suprapapillary segment of the duodenum from duodenal polyps, accessory pancreatic tissue, misplaced remnants of gastric mucous membrane, simple ulcer, Brunner's glands and the minor papilla of Santorini. However, definite proof of any such etiologic relationship is lacking. Ochsner and Wilbur stated that in their case the minor papilla of Santorini was apparently the site of origin for the neoplasm. Although such an origin is possible, this view has yet to be substantiated.

The origin of the tumor from Brunner's gland was postulated in three cases (Ramond; Vincent and Clément; Pic, and Rutishauser's case 1). In the first two no evidence was presented to substantiate this point of view. Rutishauser, however, wrote at length regarding the fine histologic changes in Brunner's glands, which led him to believe that the tumor in his case originated in these structures. In view of the fact that the postmortem examination on Rutishauser's subject was held two days after death, these histologic details would appear to be of little value. These glands were described as hyperplastic in several other cases, but as they normally vary quantitatively in different areas of the suprapapillary segment of the duodenum, the significance of this observation is debatable. Morrison and Feldman noted that these glands were numerous in the vicinity of the carcinoma in their case but were correct in interpreting this feature on the basis that the tumor originated well up in the duodenum where the glands are normally numerous. In our cases Brunner's glands were frequently destroyed by marked inflammation, ulceration and neoplastic permeation of their stroma.

Most simple ulcers are located in the first 2.5 cm. of the duodenum, and it follows that if this condition is a precancerous lesion, carcinoma should occur rather commonly in this situation, and a proportionately large number should be confined to or at least border on this area. An analysis of this series does not support this hypothesis, for in the relatively few cases in which the lesion was situated above the papilla no significant difference could be established in its occurrence in any particular portion of the suprapapillary segment. After evaluating the

evidence dealing with the association of simple ulcer and carcinoma, we are of the opinion that no proof exists to support the hypothesis that simple ulcer of the duodenum is a precancerous lesion.

AGE AND SEX; INCIDENCE

In the series of cases studied twenty-six of the patients were men (three Negroes), varying in age from 35 to 78, with an average age of about 57, and fifteen were women, varying in age from 23 to 85, with an average age of about 55.

Three of our six cases were discovered at the Jefferson Hospital in 3,526 autopsies and the others at the Philadelphia General Hospital, two between Jan. 1, 1920, and Dec. 31, 1935, 20,176 autopsies having been performed during that period.

ANATOMY

The suprapapillary portion of the duodenum extends from the pyloric sphincter to the papilla of Vater and includes, according to academic anatomy, the superior portion and the proximal part of the descending portion. The superior portion, commencing at the pylorus and measuring approximately 5 cm. in length, passes backward, upward and to the right, ending at the neck of the gallbladder. It is in relation above and in front with the quadrate lobe of the liver and the gallbladder, behind with the gastroduodenal artery, the common bile duct and the portal vein and below and behind with the head and the neck of the pancreas. The proximal descending portion, measuring from 3 to 5 cm. in length, extends from the neck of the gallbladder along the right side of the vertebral column to the papilla of Vater. It is in relation in front with the duodenal impression on the right lobe of the liver and the transverse colon; behind it has a variable relationship to the front of the right kidney in the neighborhood of the hilus; the renal vessels, the inferior vena cava and the psoas muscles below are also behind it; at its medial side are the head of the pancreas and the common bile duct; to its lateral side is the right colic flexure. The common bile duct and pancreatic duct together perforate the medial side of this portion of the intestine obliquely from 7 to 10 cm. from the pylorus. The accessory pancreatic duct sometimes pierces it about 2 cm. above and slightly in front of these.

The antrum, or *bulbus duodenale*, is a part of the superior portion of the duodenum and is directly continuous with the pylorus. In contrast to the remainder of the duodenum, its beginning portion is more freely movable and its relationship to the pancreas much looser. Schwarz has emphasized the close association of the superior portion to the stomach, both having a similar type of mesenteric fixation, similarity in behavior and appearance of the mucous membrane and similar secretory elements.

He regarded this portion of the duodenum as the "after stomach," with a smooth inner surface as differentiated from the remainder of the duodenum, which contains Kerkring folds. Åkerlund made roentgenographic studies of the stomach and duodenum in corpses, these organs being fixed in situ with formaldehyde and filled with contrast masses. Comparisons of these roentgenograms with the anatomic preparations showed that in the majority the shadow of the bulbus corresponded to the entire superior portion. Åkerlund also stated that the filling, emptying, peristalsis and tonus of the duodenal bulb are in large measure independent of the remainder of the duodenum and expressed the belief that it is an anatomic roentgenographic and physiologic entity. That portion of the duodenum from the neck of the gallbladder to the papilla of Vater is occasionally designated as postbulbar (Rutishauser).

MORBID ANATOMY

The tumor measured from 0.4 to 4 cm. in length in twenty-three cases and from 4.5 to 8 cm. in thirteen cases, and in one instance the growth involved 13 cm. of the duodenum. There was a localized growth in twenty-eight instances, thirteen of which were in the bulbar portion, eight at the superior angle and seven near the papilla of Vater. The majority of nonannular localized lesions were situated on the posterior or inferior medial wall. The suprapapillary portion of the duodenum was involved diffusely over a considerable extent in thirteen cases, the distal portion of the growth being situated near the papilla in ten, at the superior angle in two and in an indefinite location in one; the proximal margin of the growth was situated at the superior angle in four cases and in the bulbar region in nine. Neoplastic tissue was regularly found infiltrating the wall of the duodenum for varying distances, but in three cases the lesion was comparatively superficial (Herman and von Glahn and Dewis and Morse, cases 1 and 2). Opposite the primary growth a well defined tumor mass was often present on the peritoneum.

The primary growth was ulcerated in thirty instances and non-ulcerated in eight, and no mention was made of this feature in three. The ulcers were round, oval or crater-like, and in the constricting lesions there were running ulcers. Their margins were thick, rolled, broad, elevated, papillated, everted or honeycombed, and either sharply defined or irregular. The base was described in only a few instances, as gray, smooth, nodular, hard or soft, and in one it was covered by greenish red material. A superficial thrombosed or ruptured blood vessel was noted in the base of the ulcer in three cases, and in two others perforation had occurred. The ulcerated lesions were generally annular and constricting but never completely obstructive in contrast to the nonulcerated type, in half of which the lesions were almost totally stenotic.

Extension or metastases were present in thirty-one cases. This is probably a conservative figure, for in several instances only the surgical specimen was examined, and in a few others autopsy was limited to the abdomen. Adhesions to the pancreas were mentioned in sixteen cases and were inflammatory, neoplastic or both. Inflammatory adhesions were associated with local ulceration and infection and probably facilitated extension of the neoplasm. Secondary deposits in the pancreas occasionally attained a large size, measuring 6 cm. in diameter. Gross appearances suggesting tumorous infiltration of the pancreas were not always confirmed histologically (Dewis and Morse, case 3, and Pacetto), whereas other tumor foci may be only microscopic in size.

Obstruction of the common bile duct was present in eleven cases, in most of which the duct was encircled by neoplastic extensions from the duodenal lesion. In Dardinski's case there were also a few small nodules in the mucous membrane of the common bile duct at the point of obstruction. Rutishauser's case 5 is sometimes cited (Willis) as an example of intracanalicular extension along the bile ducts, but from the gross description it is evidently only another example of periductal involvement. Direct infiltration of the hepatic and cystic ducts occurred in two cases. In another (Morrison and Feldman) the growth in the duodenum compressed the hepatic duct without actually invading it. Cholecystoduodenal adhesions were observed in eight cases and were dense and fibrous in all but one, in which they were fibrinous. They were proved by microscopic examination to contain neoplastic tissue only in our case 4. The falciform ligament was infiltrated with tumor tissue in three cases.

Implantation metastases occurred as discrete nodules in six cases in the mesentery, transverse colon, gastrohepatic omentum, under-surface of the diaphragm, small intestine, pelvic wall and ovary. Rutishauser's case 1 is unique in respect to the large number of implantation metastases, and the question naturally arises whether the three small duodenal lesions regarded by him as primary may not rather have been metastatic from an unidentified source. Primary carcinoma of the prostate and thyroid glands is sometimes responsible for tumor spreads of this type and extent, but these glands were not described in Rutishauser's communication.

Cancerous involvement of the regional lymph nodes was observed in sixteen cases, in four of which the nodes in the gastrohepatic omentum, around the bronchi and in the mesentery and around the aorta were also involved. Metastatic deposits were present in the liver in eighteen cases, in the lungs in one and in the fifth and eighth dorsal vertebrae in one.

Dilatation of the stomach was mentioned in twelve cases uncomplicated by gastro-enterostomy and is considerably less pronounced a

feature than in carcinoma of the infrapapillary portion of the duodenum. Of seven cases in which the contents of the stomach were described, blood was found in four and bile in one. The mucous membrane of the stomach was atrophic in four cases and hypertrophic in one; the absence of free hydrochloric acid in the contents of the stomach in one of the former group was attributed to the atrophic condition of the gastric mucous membrane. The bowel distal to the primary duodenal lesion was distended and filled with blood in a few cases.

Generalized peritonitis occurred in two cases as a result of perforation of the duodenum. Small bloody effusions into the peritoneal cavity were observed in three instances, in each of which metastatic lesions were present on the serosa.

A single diverticulum of the duodenum was found in two cases, and in each of these the neoplastic growth occupied the margins of the sac (Bibby and Stewart; Morrison and Feldman).

In four cases there was obstruction of the pancreatic ducts with dilatation of the proximal ducts and atrophy of the parenchyma. In eight others there was chronic pancreatitis, the result in part of drainage of infected material from ulcerated lesions in the duodenum. Some degree of chronic pancreatitis may have existed prior to the development of cancer in three patients who gave an antecedent history of chronic cholecystitis.

Chronic cholecystitis was present in ten cases, in nine of which there were associated gallstones, gravel being present in the common bile duct in one, while in another a marble-sized calculus was removed from the ampulla of Vater.

The liver and bile passages showed the characteristic changes of biliary stasis in the cases of obstructive jaundice. There were dilatation of the large biliary ducts, proliferation of the small ducts, fibrosis of the portal radicles, degeneration and pigmentation of the parenchyma in the inner portions of the lobules, focal mid-zonal and biliary necroses and, in three cases, hepatic abscesses and cholangitis.

HISTOLOGY

All the cases were of the glandular type of carcinoma except one, which was of the adenosquamous variety. Acinous formation was present in thirty cases and absent in one, while it was not mentioned in ten. The acini were irregular in four cases and cystic in three; in four there was a papillary arrangement. The lesion was designated as mucinous carcinoma in three cases, and in several others considerable basophilic fibrillar material was present in and between the tumor cells and in the acini. The cells grew discretely in strands, nests or clumps in sixteen cases, in only one of which acinar structures were entirely absent. The

cells were essentially columnar or cylindric, although pleomorphism was occasionally marked, some cells being cuboidal, round, oval, polygonal or flat. Variation in size, shape and staining of the nuclei was also frequently noted, and of fourteen cases in which mitotic figures were observed they were numerous in nine and infrequent in five. The stroma, described in seventeen cases, was minimal in four and abundant in thirteen, the scirrhous character of the latter being an outstanding feature. Areas of hemorrhage and necrosis were often observed, and the connective tissue was regularly infiltrated with small round cells and occasionally with polymorphonuclear neutrophils and eosinophils. The inflammatory reaction was frequently intense about areas of ulceration and necrosis, and in one case there were multiple areas of suppuration. In Lageder's case the tumor varied considerably in the various sections, being almost entirely scirrhous in some and very cellular in others, forming acini occasionally with papillary projections, and in one section polymorphism was pronounced, hyperchromasia the rule and mitotic figures numerous. One section also showed a transformation into epidermoidal elements, with voluminous cells occurring singly and in groups of from ten to twenty or more to form large plaques, the centers of which showed fusion of cytoplasm and beginning keratinization.

Malignant transformation occurred at the margin of the ulcer in four cases and in the superficial and deeper portions of the mucosa in one case each, while in one subject the ulcerated surface was formed by muscle infiltrated by neoplastic cells, both edges of the ulcer presenting atypical glandular formation resembling somewhat the picture seen in chronic ulcer.

CLINICAL FEATURES

Onset.—The cases were divided on the basis of onset into three groups: acute onset, twenty-two; gradual onset, seventeen, and indefinite onset, two. This division was made irrespective of an antecedent history of symptoms referable to the upper portion of the abdomen, which was elicited in twelve of the cases in which the onset was acute and in four of the cases in which it was gradual.

In the cases in which the onset was acute there were many symptoms, chief among which were the following: vomiting (fourteen cases), epigastric pain (twelve), weakness and loss of weight (eleven), jaundice (six), anorexia (six), flatulence (five), belching (five), sense of pressure or weight in the epigastrium (four) and constipation (three). The duration of symptoms in eighteen of these cases ranged from one week to nine months, with an average of about three months. In three of the remaining four cases the onset occurred from three to six months before admission; the patients in two of these cases were not heard from after discharge from the hospital, and the patient in the other case died within

two years. In the other case, despite the fact that symptoms had existed for one and a half years, the onset was acute, due apparently to biliary obstruction by infiltrating carcinomatous tissue.

The duration of symptoms in the gradual group ranged from six months to four years, with an average of sixteen months. The early symptoms were pain (eleven cases), dyspepsia, heaviness or distress (eight), loss of weight (eight), vomiting (four), weakness (five), anorexia (four) and jaundice (two). An acute exacerbation or sudden change in symptomatology occurred in ten of these. The average duration of this later acute phase was two months, the clinical manifestations being vomiting (five cases), epigastric pain (five), jaundice (two) and constipation (two).

As mentioned previously, a history of antecedent illness was elicited in sixteen cases. The condition was described as disease of the biliary tract in five, gastric or duodenal ulcer in five, tuberculosis in one and indeterminate lesions of the upper part of the abdomen in six, in two of which pancreatitis and pericholecystic adhesions were demonstrated at autopsy. Of five cases with a history of disease of the biliary tract, a large duodenal diverticulum was present in one, while in the remaining four operation or autopsy revealed calculous cholecystitis.

The five cases in which duodenal or gastric ulcer was suspected were reported by Letulle, Jefferson, Ramond, Vincent and Clément, Kettle and Archibald. No conclusive evidence of the etiologic relationship between ulcer and carcinoma was advanced by these authors. In Jefferson's case posterior gastro-enterostomy was performed for relief of indigestion, epigastric pain and vomiting, and, according to the hospital records, an ordinary nonmalignant ulcer of the duodenum was found. Postoperative convalescence was satisfactory, and the patient continued in excellent health for two and a half years, when diarrhea and abdominal pain gradually developed, with loss of weight, and death occurred a year later. At autopsy a completely annular, almost totally obstructive carcinoma of the duodenum was found. In this case it seems reasonable to question the accuracy of the original diagnosis of simple ulcer, since no statement was made as to whether it was inspected directly by opening the duodenum, or whether biopsy was performed. Since obstructive phenomena were obviated by the procedure of gastro-enterostomy in this case, it is not improbable that the lesion was malignant from the onset.

Pain, Tenderness and Rigidity.—Pain was reported in twenty-eight cases, was absent in six and was questionable in three, while in the remaining four epigastric distress, soreness, a sense of pressure in the abdomen, heartburn or pain on deep palpation over the neoplasm were

the complaints. Of two patients who did not complain of pain, one was senile and the other was a morphine addict. Pain occurred early in the disease in seventeen cases and late in five, and it was likely to appear at any time of the day or night, lasting from a few minutes to several hours. It was present in the epigastrium in fifteen cases and in the lower portion of the abdomen in two and was generalized over the abdomen in one, radiating to the back in four and to the right loin and right shoulder in one each; in one case it was at first substernal and later radiated to the eleventh dorsal segment and the epigastric region. The pain was severe in six cases, intermittent or paroxysmal in nine, continuous in three and vague or variable in two. The ingestion of food preceded the onset of pain usually by from one-half to two hours in ten cases and gave symptomatic relief in two, while in three it had no effect. Abdominal tenderness was associated with pain in ten cases and was present without pain in two cases. All three patients with abdominal rigidity had pain, and one had abdominal tenderness. Pain was associated with vomiting and sour eructations in two cases, while in three others it was relieved by vomiting or belching or by the administration of alkali; in one case pain and other symptoms disappeared following cholecystectomy and choledochogastrostomy. No correlation could be established between the symptom of pain and the situation and size of the primary growth or adhesions to and neoplastic infiltrations of surrounding structures.

Vomiting.—Vomiting occurred in twenty-six cases, was absent in six and was not mentioned in nine. This symptom occurred in sixteen cases in which the onset was acute, in seven cases in which the onset was gradual at first and then became acute, in two cases in which the course was gradual throughout and in one case in which the onset was indefinite. Of the cases in which the onset was acute, vomiting was an early symptom in ten and developed later in six. Of the cases in which the onset was at first gradual and then acute, vomiting occurred with the gradual manifestations in only two and coincidentally with the acute manifestations in five. Of the cases in which the course was gradual throughout, vomiting was an early symptom in one and appeared later in another. Nausea and vomiting usually occurred together, the nausea appearing a week or so before vomiting commenced, the latter tending to become incessant terminally. Vomiting was initiated or exaggerated by food in nine cases, while in ten no such relationship was established. The vomitus contained blood in several instances, as well as particles of food which had been ingested from one to ten days previously and which sometimes exhibited evidences of putrefaction. Biliary vomiting was present in only one case in which the bile drained into the stomach

through a choledochogastrostomy opening, the operation having been performed early in the course of the disease.

Absence of vomiting was definitely stated in six instances. In the first of these the symptoms were not described in detail during an eight month interval between exploratory laparotomy and death. In another the dimensions of the primary lesion were not accurately stated. In a third the presence of a gastro-enterostomy opening obviated the effects of duodenal obstruction. In the other three cases the primary duodenal carcinoma was small, measuring, respectively, 0.6, 1.8 and 2 cm. in the greatest diameter. From this analysis it is evident that vomiting occurs regularly with the onset of intestinal obstruction but develops occasionally before there is any appreciable encroachment of the primary lesion on the lumen of the intestine. It is also possible that ulceration of the primary lesion may in some instances permit the passage of duodenal contents, and in such cases vomiting may be absent.

Jaundice.—Jaundice was present in seventeen cases, absent in fourteen and not mentioned in eight. It occurred with the acute symptoms in nine and from five to seven months after the onset in six, while in two its time of occurrence was not stated. It was due to neoplastic infiltration of the common bile duct in six cases, neoplastic obstruction of the hepatic duct in two, metastatic carcinoma of the head of the pancreas in one, pressure of the primary tumor and associated diverticulum in one and stone in the ampulla of Vater in two. In five cases the cause of jaundice was not accurately stated in the reports but was probably due to biliary obstruction. The location of the obstruction in the biliary tract depends to some extent on the segment of duodenum involved by the neoplasm; thus, in two cases in which the carcinoma originated near the pyloric orifice the hepatic ducts were obstructed, whereas neoplastic involvement of the lower end of the common bile duct was associated with tumors arising just above the papilla of Vater. Of the four cases with jaundice in which the duodenal growth was localized at the superior angle, biliary stasis resulted from neoplastic invasion of the common duct and hepatic duct (one case each), stone in the ampulla of Vater (one) and compression of the bile ducts by a combination of diverticulum and primary neoplastic lesion (one).

Jaundice was regularly associated with clay-colored stools and bilirubinuria and increased progressively in intensity unless surgical measures were instituted for its relief. In Mateer and Hartman's case the icterus index, estimated every second day for a period of two weeks, increased from 27 to 74, duodenal drainage on two occasions yielding no bile. Pain was present in eleven cases in which jaundice was present, in five there was no pain and in one this symptom was not mentioned.

Pain and jaundice occurred simultaneously in six cases, in two in association with cholelithiasis, and in five jaundice followed the appearance of pain.

Constipation and Diarrhea.—Constipation or obstipation occurred in fourteen cases and diarrhea in six cases, while in about 50 per cent the bowels were normal or there was no mention of abnormality. Constipation occurred with the onset in five cases and after the onset in three; of two cases in the former group, this symptom abated somewhat subsequently, being followed by diarrhea in one instance. Diarrhea, when it occurred, was usually persistent.

PHYSICAL EXAMINATION

A mass was palpated in the region of the primary tumor in ten cases, no evidence of a mass was detected in nineteen and there was no mention of this feature in the remainder. Although each of the following characteristics of the palpated mass was mentioned at least once, few details were available as to its size, shape, consistency, fixation, mobility, movement with respiration and continuity with liver dulness. In four cases there was associated tenderness.

It seemed of value to correlate the presence or absence of a palpable mass with the size of the local neoplasm and associated inflammatory lesions as demonstrated at autopsy. In doing this, the morbid anatomy of the condition was evaluated not so much in respect to the duodenum, pancreas, lymph nodes or serosa singly but rather in relation to the size of the lesions as a whole. For example, if the combined and associated neoplastic and inflammatory processes were extensive, the anatomic lesion was graded as large, even though the primary tumor in the duodenum was small. Of the ten cases in which a mass was palpated clinically, the anatomic lesion was graded as large in all but one. Of the cases in which a mass was not palpable or not mentioned clinically, the anatomic lesion was graded as large in sixteen cases and as small in fifteen. Local conditions may have interfered clinically with the palpation of a large anatomic lesion in seven cases, for in four there was a marked degree of rigidity or abdominal distention, in two the neoplasm was situated on the posterior wall of the duodenum and in the other there were dense local adhesions between the inferior margin of the liver and the anterior abdominal wall.

The liver or gallbladder or both were palpable in nine cases, in all of which obstructive jaundice was present. In one case the liver was enlarged and nodular and at autopsy showed metastatic nodules and biliary stasis. Dilatation of the stomach to the level of the umbilicus or symphysis pubis was noted in five cases, a succussion splash was heard in two and abdominal peristalsis was marked in three.

LABORATORY STUDIES

Analysis of the Gastric and Duodenal Contents.—Aspirated gastric contents or vomitus were examined in fourteen cases. Blood was present in eight instances and bile in one; in the latter choledochogastrostomy had been performed. Free hydrochloric acid was present in seven cases, absent in five and not mentioned in one; it was absent before and after a test meal in two, while in another it rose from 19 to 30 after this procedure. Total acidity ranged from 25 to 100 in ten cases, the average being 64. After a test meal the total acidity decreased from 87 to 45 in one case and rose from 34 to 49 in another. Duodenal drainage was carried out in only one case and yielded no bile on two attempts, the patient being jaundiced clinically; autopsy revealed obstruction of the common bile duct.

Stools.—The stools were examined in twenty-two cases, in fourteen of which blood was found either grossly or by chemical examination. The stools were acholic in nine cases, in all of which there was obstruction of the extrahepatic biliary passages. In eight additional cases of biliary obstruction, the stools contained large amounts of blood in four and were not examined in four. Typical "pancreatic" stools were found in only one case, in which the duct of Wirsung was obstructed and the duct of Santorini could not be found. In three others in which there was postmortem evidence of obstruction of the pancreatic ducts, the character of the stools was not described.

Blood Studies.—The red blood cell count or hemoglobin determination or both were reported in fourteen cases. These were normal in one case, in which, however, there was frequent vomiting, which may have produced some degree of hemoconcentration. In two cases hemoglobin estimations alone were reported and were below normal in each. In the remaining eleven cases there was marked anemia. In seven of these the color index was low, and in three it was high (1.01, 1.03 and 1.15). These findings contradict the opinion expressed by a number of authors that anemia is not a prominent feature in cases of duodenal cancer. The blood count may not be a true index of the degree of anemia, which may be masked by hemoconcentration due to dehydration incident to frequent vomiting. Loss of blood by hemorrhage occurs frequently, for blood was found in eight of fourteen specimens of gastric contents and in fourteen of twenty-two stools examined clinically; in several subjects extensive intestinal hemorrhage was demonstrated at autopsy.

Roentgenographic Examination.—The stomach and duodenum were examined roentgenographically after an opaque meal in eighteen cases, in eleven of which there was a demonstrable lesion. However, the true nature of the lesion was strongly suspected in only two cases (Mateer and Hartman, and Bastos), while in the remainder the following diag-

noses were made: ulcer (three cases), duodenal stenosis (two), carcinoma of the stomach (two) and adhesions and obstacle at the pylorus (one each). A filling defect was noted in the region of the pylorus in three cases and in the second portion of the duodenum in four, in one of which there was also a constant deformity of the duodenal cap, which was interpreted as due to displacement; in the remaining four cases no filling defect was described. The case reported by Herman and von Glahn demonstrated the value of comparing the roentgenograms with the morbid anatomic specimen. In this case the roentgenograms of the gastrointestinal tract were reported as essentially normal, and although the length of the "stalk" of barium was commented on at the time, it was interpreted as the stream passing through the pylorus. Comparison with the postmortem specimen showed that the neoplasm had formed a canal through which the gastric contents passed, and this "stalk" represented the stream of barium passing through the lumen of the duodenal growth.

There were seven cases in which no lesion was demonstrated roentgenographically. In one case aggravated vomiting interfered with the examination, and in another there was considerable retention of food. The anatomic lesions present in the remaining five cases are described briefly. In Pacetto's case there was a firm fibrous ulcerated obstruction, measuring 4 cm. in length, which involved two thirds of the circumference of the first portion of the duodenum. In Meyer and Rosenberg's case the suprapapillary segment of the duodenum was greatly narrowed by an annular papillary mass extending from just beyond the pylorus almost to the papilla of Vater. McGuire and Cornish found an infiltrating mass at the lower border of the liver and connecting with the duodenum, but the dimensions and appearance of the lesion in the mucous membrane of the duodenum were not described. In Van Tienhoven's case there was an ulcerating "brussel sprout-like" lesion on the pyloric side of the papilla of Vater, which was entirely free of neoplastic tissue. In Oschner and Wilbur's case an irregular area of ulceration, measuring 4 by 1.5 cm., was found 3 cm. below the pylorus.

It has been emphasized by others that roentgenographic studies in cases of cancer of the suprapapillary portion of the duodenum are of considerable value from a negative standpoint. Thus in patients exhibiting signs and symptoms referable to the gastro-intestinal tract, such studies may rule out the possible presence of organic lesions of the stomach, colon or gallbladder. The difficulty of visualizing carcinoma in this region can be attributed to several important factors. For one thing, the distal two thirds of the duodenum empties rapidly and is usually not entirely filled at any one time. Furthermore, as a rule it is not possible to distinguish defects in the suprapapillary segment from

deformities due to ulcer. Even with obstruction of a relatively high grade associated with a large tumor, the only significant findings may be slight alteration in the mucosal patterns as outlined by remnants of the barium. Fixation and rigidity may be of some aid in excluding a diagnosis of benign tumor but are of no value in ruling out extrinsic cancers invading the duodenum from adjacent organs and structures such as the stomach, bile ducts, gallbladder, pancreas and lymph nodes. Gastric retention in the presence of a "vacuole" in the bulb may suggest

Results in Cases in Which Operation was Performed

Year	Author	Operation	Result
1905	Gerster.....	Cholecystectomy	Died 22 hr. after operation
1906	Gelser		
	Case 1.....	Gastro-enterostomy; jejunostomy	Died 2 days after operation
1916	Jefferson.....	Gastro-enterostomy	Died 3½ yr. after operation
1920	McGuire and Cornish		
	Case 3.....	Duodenostomy	Operative recovery; discharged
1921	Van Tienhoven		
	Case 3.....	Cholecystogastrostomy	Operative recovery; discharged
1927	Morrison and Feldman	Exploratory	Operative recovery; died 7 mo. later
1928	Dewis and Morse		
	Case 1.....	8/6/26: gastro-jejunostomy; 10/21/26: resection of pylorus and first portion of duodenum	Operative recovery; discharged
	Case 2.....	Excision	Operative recovery; discharged
	Case 4.....	Choledocholithotomy	Died 6 days after operation
	Case 5.....	Excision	Died 4 days after operation
1930	Archibald.....	Exploratory	Died 21 days after operation
1931	Pacetto.....	Gastro-jejunostomy	Died 5 days after operation
1932	Mateer and Hartman	Exploratory	Died 9 days after operation
1932	Rutishauser		
	Case 5.....	Gastro-enterostomy	Died 3½ mo. after operation
1932	Cave		
	Case 8.....	2/11/14: appendectomy; 7/6/14: cholecysto-enterostomy; 10/20/14: gastro-enterostomy	Died 3 mo. after operation
1933	Eger		
	Case 1.....	12/24/31: gastro-enterostomy; 4/6/32: cholecystostomy	Died 10 mo. after operation
1934	Dardinski.....	Gastro-jejunostomy; cholecystostomy	Died 2 days after operation
1936	Stewart and Lieber		
	Case 1.....	1/2/30: cholecystectomy, choledocholithotomy and choledochostomy; 4/4/30: choledochogastrostomy; 4/14/31: gastro-enterostomy	Died 3 days after operation

tumor but does not exclude a growth at the pylorus or prolapse of the gastric mucous membrane into the duodenum.

DIAGNOSIS

A correct preoperative clinical diagnosis was made in only two cases, and in these on the basis of the roentgenographic picture (Mateer and Hartman and Bastos). A clinical diagnosis of carcinoma of the stomach or pylorus was made in eight cases, of duodenal ulcer in two, and of intestinal obstruction in two, while the following diagnoses were mentioned once: malignant obstruction of the common bile duct, carcinoma, disease of the gallbladder, carcinoma of the gallbladder or pancreas,

acute indigestion, empyema of the gallbladder, tuberculous peritonitis, calculous cholecystitis, an inflammatory process of the duodenum and probable carcinoma of the duodenum with obstruction of the common bile duct. A correct diagnosis was made at operation in ten of eighteen cases; the other diagnoses were carcinoma of the pancreas (two cases), carcinoma of the pylorus (one), fibrous obstruction of the duodenum (one) and malignant obstruction at the ampulla of Vater (one); no diagnosis was recorded in three of the surgical cases. When gastroenterostomy is done early and the malignant character of the lesion is not suspected, the subsequent clinical improvement may be so marked that a correct diagnosis is deferred until the late stages of the condition.

Early accurate diagnosis of carcinoma of the suprapapillary portion of the duodenum depends largely on thorough evaluation of the symptom complex which antedates the onset of intestinal obstruction. These early symptoms consist of vague mild complaints present intermittently for months, characterized by dyspepsia, intermittent attacks of pain, abdominal discomfort, loss of appetite and loss of weight. A mass is rarely palpable at this stage of the disease, and the roentgenographic studies are of little direct help. Later the basic symptoms in the majority of cases are those referable to intestinal and biliary obstruction. It is probable that the lumen of the intestine is temporarily obstructed for a few hours or so, followed by relief for several hours, days, weeks or even months before another attack occurs. As the disease progresses, the clinical manifestations of obstruction recur more frequently until finally nausea and vomiting develop in the vast majority of the patients. The relative incidence of the various clinical symptoms and signs and laboratory findings has been discussed under their respective headings.

TREATMENT

Reports of roentgen and radium therapy have been presented by Levin and Bastos. The results of surgical intervention in the patients in this series have not been encouraging. No instance of definite cure has as yet been recorded. As indicated in the table, seven patients died shortly after operation and four others within six months; two survived a little over a year and one two years. The subsequent fate of four patients who survived operation and were discharged from the hospital is not known. Technical considerations of the surgical treatment of carcinoma of the duodenum have recently been described by Pack and Scharnagel and Whipple, Parsons and Mullins. The difficulties that are frequently encountered may be illustrated by the fact that in the majority of cases analyzed, the process was extensive, ulcerating and constricting and frequently involved adjacent structures. In the present series, the regional lymph nodes were invaded by metastases in sixteen

cases and the bile ducts in twelve, and there were either neoplastic or inflammatory adhesions to the pancreas in sixteen cases and to the gallbladder in eight. Obviously the measures to be employed in any individual case must depend on the condition of the patient, the character and extent of the lesion and the presence and degree of intestinal or biliary obstruction.

SUMMARY AND CONCLUSIONS

This study of carcinoma of the suprapapillary portion of the duodenum represents a clinical and pathologic correlation based on six new cases and thirty-five cases reported in the literature; references to sixty-eight additional cases reported as examples of this condition are listed.

One case was found in 3,526 autopsies (0.028 per cent) and four cases in 20,176 autopsies (0.019 per cent).

The average age was 55.75 years, twenty-four of the patients being men and fifteen women.

The onset was acute in 53.6 per cent of cases and gradual in 41.4 per cent, an antecedent history of symptoms referable to the upper portion of the abdomen being elicited in approximately half of the cases in which the onset was acute and in several in which it was gradual. The symptoms occurring most frequently in the cases in which the onset was acute were vomiting, epigastric pain, weakness, loss of weight and jaundice, and the average duration of life was three and a half months. The early symptoms occurring most frequently in the cases in which the onset was gradual were abdominal pain, dyspepsia, loss of weight, vomiting and jaundice, and the average length of life after the onset was sixteen months. A marked change in symptomatology occurred in 62 per cent of the cases in which the onset was gradual, symptoms occurring which resembled those in the group in which the onset was acute. A mass was palpated clinically in the region of the primary tumor in approximately 24 per cent of the cases. The gastric or duodenal contents contained blood in eight of thirteen cases, free hydrochloric acid in seven, and bile in only one in which cholecystogastrostomy had been performed. The stools contained blood in thirteen of twenty-one cases, and nine were acholic; typical "pancreatic" stools were found in one case in which the duct of Wirsung was obstructed. A marked grade of anemia was present in ten cases, the color index being low in seven and high in three. Roentgenographic studies are of little direct value in making a positive diagnosis of carcinoma of the suprapapillary portion of the duodenum. In a few cases evidence of an ulcerated lesion in the duodenum or of obstruction of the gastro-intestinal tract was suggested but, on the other hand, extensive constricting lesions were frequently not demonstrated. Irrespective of the anatomic point of obstruction, the findings are frequently interpreted as pyloric obstruc-

tion. This method of examination is of greatest value in ruling out lesions of the stomach, colon or gallbladder.

A correct preoperative clinical diagnosis of carcinoma of the suprapapillary portion of the duodenum was made only twice. A correct surgical diagnosis was made in nine of seventeen cases, biopsy being of especial value in this connection. No instance of cure has been recorded, although follow-up studies were incomplete in a few cases.

The growth averaged 2.5 cm. in length in 56.1 per cent of cases and varied from 4.5 to 8 cm. in length in 31.7 per cent. It was localized in 68.3 per cent of cases, and in one half of these to the bulbar region. Ulceration occurred in about 73 per cent of cases, about half of these being annular or constricting lesions. Extension or metastasis occurred in 75.6 per cent of cases, to the liver, lymph nodes, pancreas, biliary passages, peritoneum, lungs and bone. All the growths were adenocarcinoma but one, which was an adenosquamous cell carcinoma.

No definite evidence has been advanced to support the hypothesis that simple ulcer of the duodenum is a precancerous lesion.

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CONCEALED HEMORRHAGE INTO TISSUES AND ITS RELATION TO TRAUMATIC SHOCK

HENRY N. HARKINS, M.D., PH.D.

AND

NORMAN W. ROOME, M.D.

CHICAGO

Evident hemorrhage, such as that from a cut vessel, with external bleeding has long been recognized as a factor of importance in traumatic shock. In certain instances during a surgical operation, when the blood is distributed on a large number of sponges, sheets and towels, the full extent of the hemorrhage is sometimes not realized. But at least it is recognized as being a factor of importance and is treated by methods intended to restore the loss of circulating fluid.

On the other hand, there are many instances in which the hemorrhage is hidden and not recognized. The shocklike symptoms that develop in patients so affected are attributed to the action of a variety of ill defined agents, such as the toxic action of traumatized tissue, anociassociation, etc. The exact relationship between the cause and the condition being indirect and uncertain, the treatment is equally indefinite. It is with the intention of showing that some of these patients suffer from hidden hemorrhage sufficient to account for their symptoms that this paper is written. Such hidden hemorrhage may be either (1) into a body cavity, such as the pleural or peritoneal cavity, or into a hollow organ, or (2) into the tissues. The first type is generally recognized as being of importance and is overlooked usually because of inability or failure to make an adequate physical examination. The second type of hidden hemorrhage is allowed to pass unrecognized in most clinical cases because its importance is not generally realized.

In experimental work on traumatic shock it was only recently that the full importance of hidden hemorrhage and extravasation of plasma into the tissues was recognized. Bayliss and Cannon¹ in 1919 performed experiments on cats wherein one hindleg was severely traumatized and the other left as a control. After death of the animal the two legs were amputated and the weights compared. There was not enough difference in weight to attribute death to hemorrhage into the tissues. Later observers, however, including Phemister,² Blalock³ and Parsons and

From the Department of Surgery, the University of Chicago.

1. Bayliss and Cannon, cited by Parsons and Phemister.⁴

2. Phemister, D. B.: The Vascular Properties of Traumatized and Laked Bloods and of Blood from Traumatized Limbs, *Ann. Surg.* **87**:806-810 (June) 1928.

3. Blalock, A.: Experimental Shock: The Cause of the Low Blood Pressure Produced by Muscle Injury, *Arch. Surg.* **20**:959-996 (June) 1930.

Phemister,⁴ repeated the experiments of Bayliss and Cannon but amputated the traumatized limb at a higher level, so as to include the loose tissue spaces of the inguinal region into which much of the extravasated blood and plasma had diffused. The difference in weight between the two hindlimbs was found by Parsons and Phemister sometimes to be as much as 60 per cent of the total volume of blood.

Division of the caudal portion of the animal into two hindquarters and variants of this method were used by other authors to demonstrate the importance of local loss of blood and plasma in other types of shock. Loss of nearly whole blood occurs in shock due to trauma to an extremity, in portal obstruction (Elman and Cole⁵) and in intestinal strangulation (Scott and Wangenstein⁶). Loss of plasma-like fluid occurs in burns (Blalock,⁷ Underhill⁸ and Harkins⁹), in freezing

4. Parsons, Eloise, and Phemister, D. B.: Hemorrhage and "Shock" in Traumatized Limbs, *Surg., Gynec. & Obst.* **51**:196-207 (Aug.) 1930.

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9. Harkins, H. N.: Shift of Body Fluids in Severe Burns, *Proc. Soc. Exper. Biol. & Med.* **31**:994-995 (May) 1934; Experimental Burns: I. The Rate of Fluid Shift and Its Relation to the Onset of Shock in Severe Burns, *Arch. Surg.* **31**:71-85 (July) 1935; The Bleeding Volume in Severe Burns, *Ann. Surg.* **102**:444-454 (Sept.) 1935.

(Harkins, Harmon and Hudson¹⁰), in intestinal trauma (Johnson and Blalock,¹¹ and Roome, Keith and Phemister¹²) and in peritoneal irrigation by hypertonic solutions (Domenech-Alsina and co-workers¹³).

REPORT OF CASES

In all cases of wounds and trauma there is some swelling. Hemorrhage occurs in some and only edema in others. In some instances this swelling may be marked and may be a vital factor. The following cases are intended to illustrate the importance of quantitative studies of the amount of swelling after trauma. The fluid present in these swellings contains a higher percentage of proteins than ordinary edema fluid, and hence its loss may lead to circulatory disturbance.

CASE 1.—Mrs. C. O'M., aged 46, had been in the hospital for three days because of a neurosis, when on March 9, 1935, at some time between 3:10 and 4 a. m., when found, she jumped out of a fourth story window, landing on a wood porch floor, a distance of 39 feet. The outdoor temperature was 27 F. at the time, and she was clad in only a thin nightgown. She was found unconscious, with a small amount of bleeding due to a laceration of the scalp. Her pulse was unobtainable, she was cyanotic and moaning and the blood pressure was not obtained for an hour and a half, when it was 60 systolic and 35 diastolic. She was given 1,800 cc. of saline solution intravenously followed by 500 cc. of blood. By 8 a. m. she was conscious, and the blood pressure had risen to 84 systolic and 40 diastolic, as shown in figure 1, but by noon it had fallen to 46 systolic, and there was a moderate cold perspiration over the upper half of the body. The red cell counts are shown in figure 1. Just before a second transfusion of 500 cc. of blood was given at 2 p. m. the count was 3,800,000. The pulse rate for two days before the accident averaged 120 (basal metabolic rate, plus 11). It ranged from 140 to 160 the first five days after the accident, and then it came down gradually to 110. The laceration of the scalp was sutured soon after the patient was discovered, and two days later roentgenographic studies revealed fractures of both innominate bones, the right ninth rib, the left radius, the right greater trochanter of the femur and the left clavicle. There were extensive ecchymoses and swellings of the right side of the chest, the right side of the abdomen and the right

10. Harkins, H. N.: Shock Due to Freezing: I. Shift of Body Fluids and Associated Blood Concentration Changes, *Proc. Soc. Exper. Biol. & Med.* **32**:432-434, 1934. Harkins, H. N., and Hudson, J. E.: Shock Due to Freezing: II. Composition of Edema Fluid, *ibid.* **32**:434-435, 1934. Harkins, H. N., and Harmon, P. H.: Experimental Freezing: Bleeding Volume, General and Local Temperature Changes, *ibid.* **33**:1142-1143, 1935.

11. Johnson, G. S., and Blalock, Alfred: Experimental Shock: XII. A Study of the Effects of Hemorrhage, of Trauma to Muscles, of Trauma to the Intestines and of Histamine on the Cardiac Output and on Blood Pressure of Dogs, *Arch. Surg.* **23**:855-863 (Nov.) 1931.

12. Roome, N. W.; Keith, W. S., and Phemister, D. B.: Experimental Shock: The Effect of Bleeding After Reduction of the Blood Pressure by Various Methods, *Surg., Gynec. & Obst.* **56**:161-168 (Feb.) 1933.

13. Domenech-Alsina, F.; Benaiges, B., and Arqué, P.: Etude du choc provoqué par l'irrigation péritonéale hypertonique, *Compt. rend. Soc. de biol.* **114**: 104-105 (Feb. 12) 1933.

arm and leg. Measurements of the right side of the body were compared with those of the left side and are shown in table 1. The maximum amount of swelling was about 1,550 cc. It is to be remembered that the left side of the body may have swelled in certain places, and there may have been some hemorrhage into the thoracic and abdominal cavities not determinable by physical examination. Furthermore, as the interval between the time the patient was last seen in her

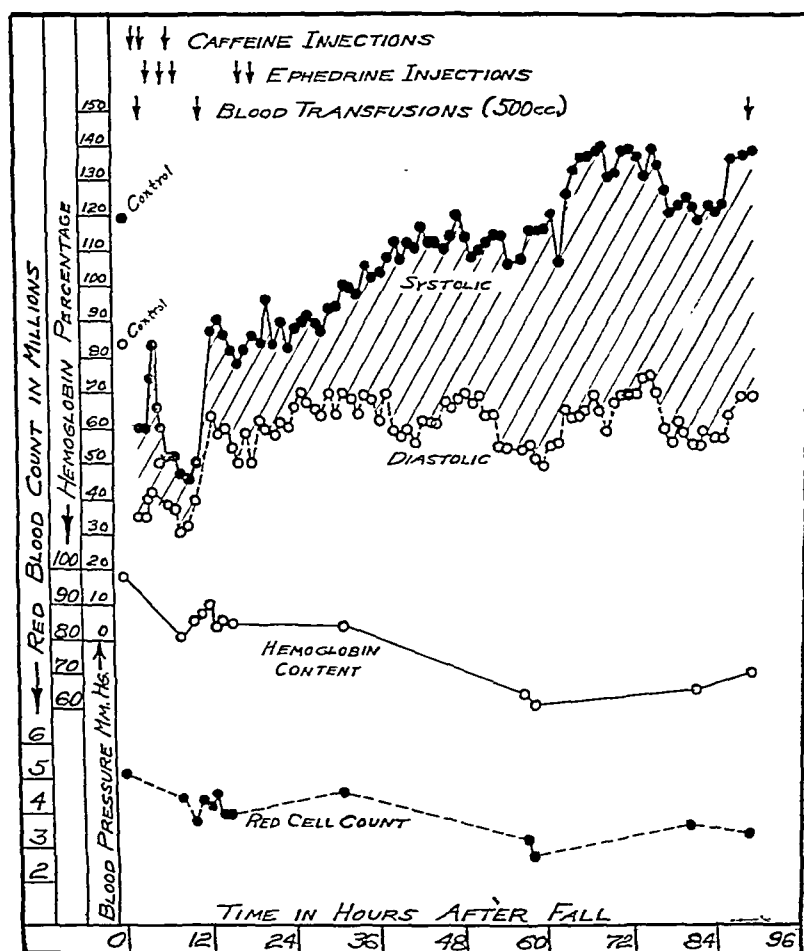


Fig. 1 (case 1).—Chart showing the course of blood pressure and blood concentration after traumatic shock associated with multiple fractures and local swelling. Injections of epinephrine hydrochloride administered subcutaneously and 1,800 cc. of physiologic solution of sodium chloride administered intravenously were given at the same time as the first injection of caffeine sodiobenzoate. The prolonged lowering of blood pressure over a period of forty-eight hours with recovery is of interest.

room and that when she was found on the porch floor amounted to fifty minutes, the effects of exposure to cold have to be considered. The first comparative

measurements were recorded twelve hours after the accident. Other readings taken almost daily during the next two weeks showed no further swelling. Nine days after the accident the asymmetry began to disappear; in twelve days it had almost disappeared, and two weeks after the injury measurements on the two sides were about equal. The measurements were taken at different points, and the volume was calculated for each segment as that of a frustum of a cone. A rough estimate of volume is thus derived from the well known formula:

$$V = 1/3 \pi h (r_1^2 + r_2^2 + r_1 r_2)$$

In this patient the steady fall in the red cell count despite the absence of continued external hemorrhage and of known hemorrhage into the visceral or body cavities is of interest. Continued hemorrhage into the injured tissue spaces may have been a factor. Restoration of the blood volume by an inflow of fluid from the noninjured tissues in remote parts of the body is another possible cause.

TABLE 1.—*Measurements of Arms, Leg and Body in Case 1**

Point of Measurement	Right Side		Left Side	
	Circumference, Cm.	Volume, Cc.	Circumference, Cm.	Volume, Cc.
5 cm. above elbow.....	29.0	308	28.5	292
Elbow.....	26.5	270	25.5	244
5 cm. below elbow.....	25.5		24.0	
22 cm. above patella.....	59.5	2,390	55.5	2,070
12 cm. above patella.....	49.5	3,060	46.0	2,730
12 cm. below patella.....	30.5		29.5	
Semicircumference of abdomen...	42.0	5,605	39.0	4,845
Total.....		11,633		10,181
Excess.....		1,552		

* The excess volume of the right arm is inappreciable, while that of the right leg and the right side of the body is considerable. It is not known, however, that the opposite limbs or portion of the abdomen were of normal size. The volume of the halves of the abdomen is calculated as that of a half of a cylinder with the semicircumference given, and a length of 20 cm., that is, approximately the extent of the ecchymotic region on the right side. The excess of 1,550 cc., if composed of blood or plasma, would be a factor of importance in the production of traumatic shock.

CASE 2.—Mrs. C. L., aged 42, received fractures of the left femur, left tibia and both bones of the left forearm just before admission to the hospital. The volume of about two thirds of the left thigh was 8,900 cc. by measurement and of a corresponding portion of the right thigh 7,100 cc., representing a swelling of 1,800 cc. However, since there was 1.5 cm. shortening of the thigh due to fracture, using the average circumference of the thigh as 50 cm., the corrected swelling was 300 cc. less, or about 1,500 cc. This did not include the swelling of the arm or tibial region. A good portion of this swelling was present within a few hours after the injury; it was somewhat more marked in three days and had absorbed to some extent in ten days.

The blood pressure was 94 systolic and 68 diastolic two hours after the patient's admission, and she was given a transfusion of 650 cc. of blood immediately and a similar transfusion four days later. The red cell count was 3,900,000, the hemo-

globin content 70 per cent (Sahli) and the hematocrit reading 34 on the day of admission (after a blood transfusion). The red cell count two days later was 2,600,000 and gradually rose thereafter.

CASE 3.—Mrs. J. L., aged 51, entered the hospital an hour and a half after a severe automobile accident with fractures of the shaft of the left femur, the right tibia and the fibula in two places (the upper and the lower third), both bones of the right forearm, the right innominate bone, a 3 inch incised wound of the scalp and a jagged 5 inch incised wound of the wall of the lower part of the abdomen. The amount of hemorrhage from the external wounds had been relatively small, while there was great swelling around the sites of the fractures. These swellings were not measured. There were no specific signs of fat embolism. The blood pressure on admission was 60 systolic and 40 diastolic, and after the administration of 1,500 cc. of Ringer's solution intravenously, it rose to 114 systolic and 74 diastolic five hours after the accident. It remained around 120 systolic until forty-eight hours after the accident, when it fell to 98 diastolic and 60 systolic. Transfusion of 500 cc. of blood restored it to normal, where it remained. The

TABLE 2.—*Changes in the Blood Concentration in Case 3*

Time	Hemoglobin Content	Red Cell Count, Millions
On admission.....	93	5.2
14 hours later.....	85	4.3
18 hours later.....	60	3.4
36 hours later.....	..	3.7
48 hours later.....	55	2.9
50 hours later.....	Blood transfusion, 500 cc.	
60 hours later.....	60	3.2
64 hours later.....	58	2.9
84 hours later.....	60	3.5
108 hours later.....	60	3.9
160 hours later.....	65	4.2

hemoglobin content and the red cell count fell steadily over the forty-eight hour period before the blood transfusion, despite the fact that all external hemorrhage was controlled, and there was no demonstrable hemorrhage into the body cavities or viscera.

Continued hemorrhage into the tissues at the sites of injury on the one hand and secondary effects of restoration of blood volume by inflow of tissue fluids at places remote from the injuries on the other hand are possible explanations of this continued dilution of blood just as in case 1. The blood changes are shown in table 2. Technical errors in determination of the hemoglobin percentage and red cell count undoubtedly account for some of the minor variations.

CASE 4.—Mrs. C. S., aged 58, was admitted to the hospital with multiple fractures, a blood pressure of 50 systolic and 40 diastolic and the typical picture of traumatic shock following an automobile accident.¹⁴ Despite blood transfusion and the administration of other fluid intravenously, she died eight hours after admission. Necropsy revealed a loss of about 1,200 cc. of blood at the site of

14. This case has previously been reported in full by Wilson, H., and Roome, N. W.: *Am. J. Surg.* 22:333-334 (Nov.) 1933.

numerous fractures and from traumatic rupture of the aorta. In this case the concealed hemorrhage was partly into the tissues and partly into the pleural cavity and the mediastinum.

CASE 5.—Mr. J. P., aged 34, underwent a disarticulation of the hip for chronic osteomyelitis of the femur and suppurative gonitis on June 5, 1935, with a blood pressure reaction (fall to 96 systolic and 78 diastolic an hour after operation with prompt recovery). Twelve days later the patient became much worse, and it was found that he had bled about 1,000 cc. into the amputation stump. The blood pressure had again fallen to 98 systolic and 52 diastolic. He was given two blood transfusions totaling 1,000 cc. that day, with a rise in pressure to 105 systolic and 74 diastolic and eventual recovery. Marked edema involving especially the face disappeared soon after the transfusions and may have been due to a low level of plasma protein.

CASE 6.—Mrs. C. M., aged 30, caught her right hand and the lower half of the forearm under a folding sofa. Because she was alone in the house, it was five

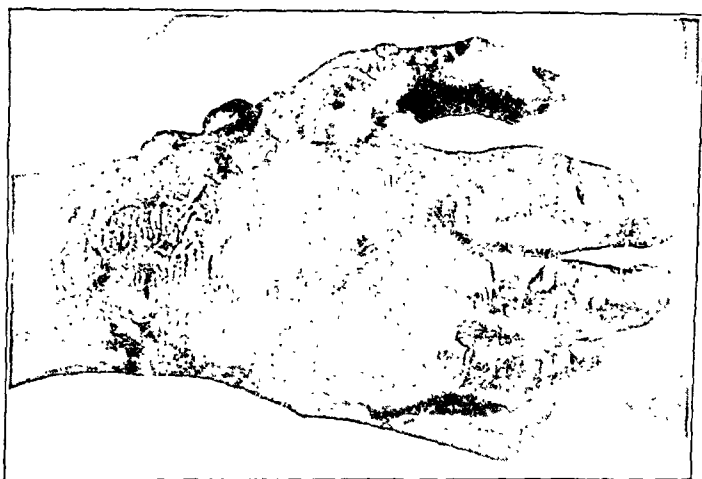


Fig. 2 (case 6).—Extreme swelling of hand of patient C. M. taken eighteen hours after the accident.

hours before she could be released. On admission to the hospital soon after, the hand appeared as shown in figure 2 with huge blisters. The blister fluid contained amounts of nonprotein nitrogen and sodium chloride similar to the composition of blood plasma, and it clotted spontaneously. The volume of the hand and forearm, as measured by a plethysmograph twelve hours after admission, was 600 cc. greater than the volume of the left hand and forearm. The red cell count at that time was 7,100,000, and the hemoglobin content was 95. The next day the red cell count was 6,600,000, and five days after admission it was 4,700,000. The blood pressure remained normal throughout. It seems unlikely that this amount of swelling could have produced all the blood concentration.

CASES 7-10.—These four cases represent instances of minor injuries in which quantitative measurement of the resultant swelling was made. In none of them was the trauma sufficient to cause shock, a fall in blood pressure or changes in the concentration of blood. Jack F., aged 4 years, had an increase in the size of the left thigh (measurement) of 200 cc. six hours after receiving a fracture of the left femur. Mrs. J. M. and Mrs. F. W. each ran her left arm through a wringer almost to the elbow. The first patient had a swelling of 260 cc. (measurement)

and 300 cc. (plethysmograph) and the second patient of 250 cc. (measurement). The readings in both instances were taken twelve hours after the injury. Two hours after a fracture of both bones of the right leg, Mrs. McM. had a swelling of 300 cc. (measurement) of the affected leg.

COMMENT

In some of the cases reported here concealed hemorrhage into tissues followed injury of such a slight degree that the loss of blood was not great enough to lead to shock. In only one case (case 4) did death result, and in this instance there was in addition bleeding into a body cavity and external bleeding. However, the lesson learned from the minor injuries of the group, namely, that there may be considerable loss of blood into the tissues which is not visible on casual examination, can be applied to more serious injuries. If a simple crushing of the hand and forearm can produce an increase in the local volume of several hundred cubic centimeters in a few hours, more extensive body injuries could easily produce a change of several times that much.

The measurements of circumferences of the limbs and body and subsequent calculation of the difference in volume on the two sides from the volumes of a series of frusta of cones is not expected to be an exact quantitative method. However, check measurements usually agreed quite well, and the volumes calculated were in all instances greater on the injured side. In one case a check reading was made by the plethysmographic method which agreed well with the calculated volume difference. In another instance only the plethysmographic reading was taken.

In most instances the swelling appeared rapidly in the first few hours after injury. After reaching a maximum, it took several days to subside. The relative amounts of extravasated blood and plasma constituting the swelling was variable with the injury, but as no incisions into the swollen areas were made or analyses performed, the exact proportions were uncertain. Local discoloration and lack of marked blood concentration would indicate that in those cases at least a good share of the swelling was due to a loss of whole blood.

This proportionate loss of whole blood and plasma in certain traumatic forms of secondary shock has led to some confusion in the literature. Coonse, Foisie, Robertson and Aufranc¹⁵ stated that traumatic shock is accompanied by blood concentration and hemorrhagic shock by anemia. Moon¹⁶ cited the same differentiating point between the two

15. Coonse, G. K.; Foisie, P. S.; Robertson, H. F., and Aufranc, O. E.: Traumatic and Hemorrhagic Shock: Experimental and Clinical Study, *New England J. Med.* **212**:647-663 (April 11) 1935.

16. Moon, V. H.: The Shock Syndrome in Medicine and Surgery, *Ann. Int. Med.* **8**:1633-1648 (June) 1935.

types of shock. It is probable that the time element alone is one of the chief factors differentiating the two types. In acute hemorrhage the loss of blood is sudden in many instances, and at death what Moon calls a "dry necropsy" is found, the tissues being anemic. With a slow leak of blood into the tissues, the blood pressure is maintained at a low level for a prolonged period of time (as in case 1). This prolonged lowering of the blood pressure alone will give rise to increased permeability of capillaries and to certain organic changes typical of Moon's "wet necropsy" that he says accompanies shock. Even Coonse and his collaborators¹⁵ admitted that slow hemorrhage simulates traumatic shock. In many types of shock, furthermore, especially after burns or experimental intestinal manipulation, the loss of fluid is almost entirely blood plasma, and naturally hemoconcentration results. In other types of shock, such as after physical trauma to an extremity, both whole blood and plasma may be lost, and at the other end of the scale stands simple hemorrhage in which only whole blood is lost. Consider for the minute a hypothetical closed vascular system containing 5 liters of blood and with a hematocrit reading of 50 per cent: 1. If 2 liters of plasma is lost the relation will be 2,500 cc. cells and 500 cc. of plasma, and the hematocrit reading will rise to 83; later, if tissue fluids restore this loss of fluid, the hematocrit reading will again drop to 50. 2. If 1 liter of whole blood and 1 liter of plasma are lost, the relation will be 2,000 cc. cells and 1,000 cc. of plasma, and the hematocrit reading will be 67. With varying proportions of loss of whole blood and plasma, the hematocrit reading will approach normal. In actual practice, it may be below normal, and a relative anemia will result due to inflow of tissue fluids. 3. Finally, if whole blood is lost, there is no change in the hematocrit reading in a hypothetical closed system, but the accompanying inflow of tissue fluids will theoretically always produce anemia. Elman, Weiner and Cole¹⁷ have shown experimentally that with local anesthesia hemorrhage produces anemia but that with amytal anesthesia there may even be concentration of the blood after hemorrhage. Blalock³ concluded his discussion of this aspect of the question by saying that "there may be two types of hemorrhage, that outside the body . . . and that into the tissues."

Concerning Crile's¹⁸ report of slight change or leukopenia in shock and leukocytosis in hemorrhage, in several of the cases presented in

17. Elman, R.; Weiner, D. O., and Cole, W. H.: Effects of a General Anesthetic (Sodium Amytal) on the Erythrocyte Count Following Hemorrhage, *Proc. Soc. Exper. Biol. & Med.* **32**:793-796, 1935.

18. Crile, G. W., cited by Orr, T. G.: Hemorrhage and Traumatic Shock, in Lewis, Dean: *Practice of Surgery*, Hagerstown, Md., W. F. Prior Company, Inc., 1935, vol. 1, chap. 9, p. 2.

this paper marked leukocytosis developed after injury; for example, case 1, 33,000; case 2, 19,000; case 3, 28,000, and case 4, 28,000.

SUMMARY AND CONCLUSIONS

External hemorrhage has long been recognized as producing secondary surgical shock; concealed hemorrhage into the body cavities and hollow organs has been recognized but is often not diagnosed, while concealed hemorrhage into tissue spaces has not been universally considered as an important clinical cause of secondary shock.

Cases of concealed hemorrhage and extravasation of plasma into tissue spaces are presented. The resultant swelling is usually greater when measured quantitatively than casual physical examination would have led one to believe.

The extensive concealed hemorrhage and plasma extravasation in clinical cases substantiates the experimental observations of others that such local loss of fluid from the circulating blood stream is a factor of importance in the production of secondary surgical or traumatic shock.

IODINE CONTENT OF BLOOD IN CHOLECYSTIC DISEASE

JOSEPH L. DECOURCY, M.D.

CINCINNATI

That normal human blood contains iodine is a matter of rather recent observation, although its presence has been suspected for many years. One of the earliest treatments for goiter was with burnt sponge, and when early in the nineteenth century it was demonstrated that sponges are rich in iodine, the employment of this drug in the therapy of goiter came about inevitably. It was in 1820 that the Swiss physician, Coindet,¹ made this clinical application. From that day to this, iodine has been the standard pharmaceutical weapon against all forms of depletion of the thyroid gland.

Yet three quarters of a century elapsed before it was discovered that the thyroid gland is itself an iodine factory. The iodine content of the normal thyroid gland was demonstrated by Baumann² in 1895, and this discovery led chemists and biologists to endeavor to find out if iodine existed in other body tissues, though for many years thereafter the thyroid gland and its diseases formed the center of interest. In the United States public health workers and even agricultural chemists became intensely interested in the question of iodine deficiency and the normal distribution of iodine in living tissues. Working with domestic animals, David Marine and his colleagues determined the iodine content of the thyroid glands of different species, confirming Baumann's earlier assertion that the pathologic thyroid gland always has a low iodine content. Other investigators, among whom may be mentioned Cameron, Forbes, Fenger and McClendon, made many estimations of the amount of iodine contained in such materials as food and drinking water.³

There remained, however, the constant difficulty of making accurate estimations, because no method had been developed sufficiently delicate

From the Department of Surgery, the DeCourcy Clinic.

1. Coindet, J. F.: Découverte d'une nouveau remède contre le goître, *Ann. de chim. et phys.* **15**:49, 1820.

2. Baumann, E.: Ueber das normale Vorkommen von Jod im Thierkörper, *Ztschr. f. physiol. Chem.* **21**:319, 1895.

3. Orr, J. B., and Leitch, Isabella: Iodine in Nutrition, Medical Research Council, Special Report Series, no. 123, London, His Majesty's Stationery Office, 1929.

to determine the minute quantities of iodine which are normal to most plant and animal cellular structures. This was especially true of the iodine content of blood.

DETERMINATION OF THE IODINE CONTENT OF BLOOD

When in 1922 the Swiss Goiter Commission, recognizing this need, requested the government bureau of hygiene to attempt the production of a better method, von Fellenberg,⁴ of the bureau's personnel, was set to work on the problem. He succeeded in perfecting "a true micro-method for the determination of iodine," the lower limits of which were about one ten thousandth of a milligram (0.0001 mg.).

Among von Fellenberg's associates at Bern, where the experiments were conducted, was Sturm,⁵ a Bavarian. After learning von Fellenberg's method, he returned to Veil's clinic at Munich, where he made numerous studies not only on the blood of patients with goiter (in whom he was primarily interested) but likewise on the blood of normal persons and of persons ill with diseases other than those involving the thyroid gland. Another student of von Fellenberg, Lunde,⁶ of Oslo, Norway, further developed the master's method and in his own country studied the iodine content of the blood in normal and in thyrotoxic persons. Sturm's study was really the first noteworthy contribution on the subject of iodine values in human blood. Kendall and Richardson,⁷ whom Orr and Leitch⁸ credit with having presented "the first modern figure for blood iodine," had employed ox blood for most of their determinations, although a few samples of human blood had been tested prior to 1920.

The work was soon greatly extended, and determinations were made of the iodine content of the blood in many other diseases besides those of the thyroid gland. Factors influencing the results, the existence of which had been previously ignored, such as geographic location and season of the year, were now taken into consideration, and the results were judged accordingly. Thus Curtis and his collaborators⁸ found:

The average normal iodine content of human blood in Chicago is about 12 γ per hundred cubic centimeters. This level falls during the winter months. It is

4. von Fellenberg, T.: Das Vorkommen der Kreislauf und der Stoffwechsel des Jods, *Ergebn. d. Physiol.* **25**:176, 1926.

5. Veil, W. H., and Sturm, A.: Beiträge zur Kenntnis des Jodstoffwechsels, *Deutsches Arch. f. klin. Med.* **147**:166, 1925.

6. Lunde, G.; Closs, K., and Pedersen, O. C.: Untersuchungen über den Blutjodspiegel bei der primären Thyreotoxikose, *Biochem. Ztschr.* **206**:261, 1925.

7. Kendall, E. C., and Richardson, F. S.: Determination of Iodine in Blood and in Animal Tissues, *J. Biol. Chem.* **43**:161, 1920.

8. Curtis, G. M.; Davis, C. B., and Phillips, F. J.: Significance of Iodine Content of Human Blood, *J. A. M. A.* **101**:901 (Sept. 16) 1933.

elevated during early menstruation and pregnancy. It is higher if the person is taking iodized salt regularly. In fact, many observations show that it is elevated by any form of iodine medication that has thus far been studied. Owing to the minute amount of iodine normally present within the blood, a special term of designation has been widely adopted. This, a gamma (γ) or microgram, is 0.001 mg. Thus, 100 cc. of human blood normally contains 0.012 mg. of iodine. The total iodine contained in the entire human blood stream is consequently less than 1 mg.

These same investigators, whose work was done at the Billings Hospital, Chicago, made observations on patients in that institution suffering from diseases other than those of the thyroid gland and also on normal, healthy members of the hospital staff. "The majority of hospital patients present a normal blood iodine," they wrote. "Among the diseases investigated were tuberculosis, chronic osteomyelitis, fractures, and Hodgkin's disease. The blood iodine is normal in patients with cancer. There are, however, two striking exceptions. In acute severe infections, as in septicemia, the blood iodine is elevated. It is likewise elevated in lymphatic leukemia." They concluded that the level of the iodine in the blood is controlled by the activity of the thyroid gland, and in disease of the gland, at least, the significance of the iodine content "is similar to that of the blood sugar in diabetes mellitus, and to that of blood calcium in parathyroid disease."

Yet as late as 1931, Orr,⁹ who had spent a considerable time in the investigation of all methods then extant, remarked rather sadly:

It has been made clear that the present methods in use for the estimation of iodine in very minute quantities and in the presence of organic materials are so unsatisfactory as to impede further progress in research. There is need for a standard method of estimation, suitable for use by all workers alike, that will give results closely approximating to accuracy, or results in which the standard error is constant and known.

Notwithstanding these difficulties, the importance of estimating the iodine content of the blood was more and more impressed on those members of the medical profession who had to deal with diseases of the thyroid gland. The need was particularly felt in the so-called "goiter belt" in the Eastern Central portion of the country. After 1923, when von Fellenberg's method—a great improvement on any previously tried—was introduced, more progress became possible. Other ways of estimating small iodine contents were put forward by Leitch and Henderson¹⁰ and by McClendon.¹¹

9. Orr, J. B.: Iodine Supply and the Incidence of Endemic Goitre, Medical Research Council, Special Report Series, no. 154, London, His Majesty's Stationery Office, 1931.

10. Leitch, I., and Henderson, J. M.: Estimation of Iodine in Foodstuffs and Body Fluids, *Biochem. J.* **20**:1003, 1926.

11. McClendon, J. F.: The Determination of Traces of Iodine, *J. Am. Chem. Soc.* **50**:1093, 1928.

Late in 1932 Davis and Curtis¹² made use of the fact discovered by Winkler in 1916—that an iodide may be readily oxidized to an iodate. Using bromine for this oxidation, they were able to make quantitative determinations on the iodine content of the blood far more exact than any previously obtained. But as they admitted, the method “is by no means an easy one,” requiring “experience and practice to obtain satisfactory results.” The estimation of the iodine content of blood remains, therefore, a procedure which is not carried out as often as it might be for the good of the individual patient as well as for the orderly progress of an interesting and clinically valuable branch of medical science.

IODINE CONTENT OF BLOOD IN DISEASES OF THE GALLBLADDER

With the establishment of relatively simple and accurate means of determining the iodine content of blood, therapeutists were able to make practical clinical use of this valuable addition to their diagnostic equipment. Confined almost exclusively at first to disturbances of the thyroid gland, the value of determinations of the iodine content of blood in other disease conditions was soon demonstrated. For the past year and a half my associates and I have been making routine studies of the iodine content at the DeCourcy Clinic. Employed originally only in connection with goiter work, in endeavoring to arrive at a normal standard for the geographic area within a hundred miles of Cincinnati, we made more than two hundred determinations on the blood of patients suffering from other diseases as well.

In the course of these routine tests we found that the iodine content of the blood is markedly increased in cases of cholecystic disease of long standing and in cases of hepatic deficiency. We later found that in cases of acute cholecystitis there is always a high iodine content. After we had determined the normal to be from 3 to 6 micrograms per hundred cubic centimeters of blood, the following figures were obtained as an average in cases of disturbances of the liver and gallbladder:

Chronic cholecystitis with stones (20 cases).....	16.6 micrograms
Hydrops of the gallbladder (4 cases).....	13.6 micrograms
Carcinoma of the liver (3 cases).....	650.00 micrograms
Chronic cholecystitis (stone in the common duct) (5 cases) ..	2,090.00 micrograms

In cases of chronic cholelithiasis the figure before the administration of dextrose was 110 micrograms. After the administration of 1,500 cc. of 5 per cent solution of dextrose the figure fell to 86.7 micrograms. All determinations were made in duplicate and are accurate within 0.2 microgram.

12. Davis, C. B., and Curtis, G. M.: Blood Iodine Studies: Quantitative Determination of Iodine Content of Blood, *J. Lab. & Clin. Med.* **18**:24, 1932.

A study of these results leads inevitably to the conclusion that the liver plays an important rôle in the metabolism of iodine. In practically all our cases of cholecystic disease of long standing as well as in the acute fulminating type the iodine content of the blood was abnormally high.

ALIMENTARY VARIATION IN IODINE CONTENT OF BLOOD

This aspect of the study of the iodine content does not seem to have received much attention from investigators. In 1933 Elmer and Luczynski¹³ presented to the Biological Society of Lwów, Poland, a short note on the excretion of iodine in the bile in the fasting subject and within a short time after meals.

According to Elmer and Luczynski, certain authors (Y. Maruno) have maintained recently that in rabbits there is no physiologic incorporation of iodine in the bile. Nevertheless, many other investigators have found that physiologic iodine is present in rabbits' bile. But as the amounts found by these different workers vary greatly, it is evident that its presence in the bile must be very inconstant, ranging between wide limits, with the possibility of high values being reached under certain conditions. By contrast, in the blood there is always a relatively fixed amount of iodine, the highest figures never surpassing 20 micrograms per hundred cubic centimeters of blood. In the bile of rabbits have been found values varying from 15 to 62 micrograms per hundred cubic centimeters of blood (Maurer and Ducrue); in the bile of cattle, from 3.4 to 32.5 micrograms (Pfeifer), and in the bile of dogs, from 13 to 113 micrograms (Schittenheim and Eisler). The reason for such wide variations should be ascertained. It is noteworthy that not one of these investigators has mentioned whether the estimations were taken before or after meals.

With a view to establishing the normal ratio of the iodine in the bile to the other constituents of this body fluid for a twenty-four hour secretion period, the technic previously described was used in experiments on twelve rabbits. Bile was collected from nine rabbits during the fasting period (at least from twelve to fifteen hours after the last meal) and from three other rabbits immediately after eating (the ration consisted of beet roots, hay and oats). The values for the iodine content of bile obtained during fasting and that of bile examined immediately after the taking of food are widely different. This difference depends evidently on whether the bile is tested after fasting or after the ingestion of food. The values obtained after fasting have a rather narrow range (from 4 to 14 micrograms per hundred cubic centimeters

13. Elmer, A. W., and Luczynski, Z.: L'excrétion d'iode par la bile, à jeûne et après le repas, *Compt. rend. Soc. de biol.* **114**:1340, 1933.

of bile), being similar to those obtained for blood. The values for iodine obtained directly after eating are always higher (from 27 to 69 micrograms). Thus it is perfectly evident that the amount of physiologic iodine present in the bile at any given time will be greatly influenced by alimentation, which is diametrically opposed to the behavior of iodine in the blood. For example, in one instance bile examined three hours after eating gave values of 55 micrograms per hundred cubic centimeters of blood, but five hours later the values had fallen to 34 micrograms.

In regard to the twenty-four hour excretion of iodine in the bile, the studies of Elmer and Luczynski gave values of from 2.8 to 26 micrograms during fasting and of from 20.7 to 82.2 micrograms after eating.

There is strong evidence, therefore, that the marked variations in the values for the iodine content of bile, their sudden and violent upward fluctuations, as noted by the aforementioned investigators, are influenced not only by seasonal and age conditions but by the time (fasting or after feeding) when the specimens to be tested are secured.

Finally, it must be admitted that the liver plays an important rôle in the metabolism of iodine and that immediately after food enters the digestive tract the liver acts to eliminate the iodine constituents by way of the bile.

In conclusion, Elmer and Luczynski proved that the amount of iodine in the bile is sharply influenced by alimentation. During fasting the values remain within comparatively narrow limits (from 4 to 14 micrograms per hundred cubic centimeters of bile). On the other hand, after eating the values rise sharply (as high as 69 micrograms). Therefore, the liver plays an important and immediate rôle in the metabolism of iodine.

The part played by the liver in the metabolism of iodine continued to interest Elmer and Luczynski,¹⁴ for somewhat more than a year later a second note on their observations was published. They continued to study the behavior of iodine simultaneously in both blood and bile, in the fasting state and after the taking of food. In experiments on five rabbits, the iodine in the blood was estimated after a twenty-four hour fast. The iodine in the bile after fasting was not measured, but was estimated on the basis of median values derived from previous experiments on nine rabbits. The figures for the iodine content of the bile after fasting did not range between very wide limits; their minimum was 9.2 micrograms per hundred cubic centimeters of bile, closely approximating those for the iodine content of the blood.

14. Elmer, A. W., and Luczynski, Z.: Rôle du foie dans la régulation du taux de l'iode dans le sang, *Compt. rend. Soc. de biol.* **115**:1717, 1934.

After examinations were made of the blood during fasting, the animals were given a twenty-four hour alimentation of beet root, oats and hay. The bile was collected ninety minutes after the last feeding. At the same time a sufficient quantity of blood was obtained. The figures obtained show that the iodine content of the blood did not rise to any great extent (from a minimum of 13.2 micrograms up to 16.4 micrograms per hundred cubic centimeters of blood), while the iodine in the bile, on the contrary, showed a marked rise after the taking of food (from 9.2 micrograms to 45 micrograms).

It is evident that alimentary iodine is eliminated into the digestive tube, principally by the liver through the bile. In following up the fate of this iodine in the digestive canal, one is impressed by the fact that iodine appears in but very minute quantities in the stools. The amount of iodine excreted in the stools of experimental animals, all of which were on the same diet, varied from 2 to 11 micrograms in the twenty-four hours. The amount excreted in the bile far exceeds this, as the figures for iodine in the bile ranged between 32 and 82 micrograms in twenty-four hours.

One is forced to the conclusion that this divergence between the excretion of iodine in the stools and its excretion in the bile can be explained only by resorption by the blood stream of the iodine originally excreted into the digestive tube with the bile. The iodine thus enters the portal vein and completes a continually repeated cycle: from the digestive canal to the portal vein, from the portal vein to bile, from bile to the digestive canal and so on ad infinitum.

One might theorize that during the first stage of this cycle, when the iodine enters the circulation after a meal, the liver does not permit the iodine to accumulate in the blood until it reaches a high value; and that in proportion as the alimentary hyperiodemia (excess of iodine in the blood) is lowered, the iodine is once more resorbed into the digestive canal. Without doubt, the liver plays the part of regulator of the proportion of iodine in the peripheral blood in that it forces throughout the entire circulation the maintenance within comparatively narrow limits of a nicely adjusted balance of iodine in the blood.¹⁴

CLINICAL CONFIRMATION

The findings of these Polish investigators have been closely duplicated in my own clinic. In making our determinations we have used the method described by Trevorrow and Fashena¹⁵ in 1935. As already stated, our original object was to obtain diagnostic aid in determining the extent of the thyrotoxicosis in our patients with goiter. We were

15. Trevorrow, V., and Fashena, G. J.: Determination of Iodine in Biological Material, *J. Biol. Chem.* **110**:29, 1935.

sadly disillusioned after the idea had been put into practice for some time, because, although some patients suffering from hyperthyroidism did show an increase of iodine content of the blood, others—and the condition of some of them was as grave as that of any patients we have seen—gave values well within normal limits. This happened even when myxedema was in evidence. In our experience the results of the test for the iodine content of the blood in cases of goiter are sadly confusing when compared with the dependence we are able to place on the basal metabolism readings.

These findings have led us to the conclusion that iodine deficiency may not be the causative factor in the production of goiter, and the results obtained by others would seem to point in the same direction. The average ratio of inorganic to organic iodine in the cases in the clinic is 17 per cent. In reports from European clinics it averages 1:2. All our results emphasized the importance of the liver in the metabolism of iodine.

SUMMARY

The conclusion drawn from our studies and clinical applications was that determination of the iodine content of the blood might be a better test of hepatic function in cases of cholecystitis of long standing than the dye tests now in general use. This is because the liver is here working with a normal constituent of the blood, whereas when dyes are introduced artificially, as in the bromsulphthalein test, the introduction of a foreign element may well cause abnormal responses by the liver and disturb function appreciably. At present we are administering dextrose for several days before operation to all our patients with diseases of the gallbladder who have a high iodine content of the blood. This we believe to be far more effectual in preventing "liver deaths" than the administration of dextrose postoperatively. We have not yet been able to judge from the iodine content as to the most favorable time for performing operation, but are tentatively assuming that when it is below 100 micrograms per hundred cubic centimeters of blood one may operate with reasonable safety.

HEADACHE AFTER SPINAL ANESTHESIA

HARRY KOSTER, M.D.

LOUIS P. KASMAN, M.D.

AND

ARTHUR SHAPIRO, M.D.*

BROOKLYN

Various explanations have been given for the postoperative headache which occasionally follows spinal anesthesia. Most of them can be classified under the headings of: (a) seepage of cerebrospinal fluid after spinal puncture,¹ (b) irritative meningitis² and (c) contamination of the material injected, causing irritation of nerve tissue.³

Recently considerable has been said regarding factors which render the anesthetic agent irritating to nerve tissue and thus produce post-operative headache.^{3a} It has been claimed that contamination by antiseptic solutions used for sterilization of the skin (needle puncture through skin dripping with iodine) caused headache; also that hypertonicity resulting from dissolving crystals of procaine hydrochloride in cerebrospinal fluid was a potent factor in the production of headache. Further, it has been stated that the p_H of the solution is also important.

* Dr. Henry Lerner Fellow.

From the Richard Morton Koster Research Laboratory, Crown Heights Hospital.

1. (a) Peluse, S.: Post-Spinal-Anesthetic Headache, Illinois M. J. **67**:372, 1935. (b) Evans, C. H.: Possible Complications with Spinal Anesthesia: Their Recognition and Measures Employed to Prevent and to Combat Them, Am. J. Surg. **5**:581, 1928. (c) Nelson, M. O.: Postpuncture Headaches: A Clinical and Experimental Study of the Cause and Prevention, Arch. Dermat. & Syph. **21**: 615 (April) 1930. (d) Heldt, T. J.: Lumbar Puncture Headache, M. J. & Rec. **129**:136, 1929. (e) Weinstein, M., and McHugh, J. P.: One Thousand Cases of Spinal Anesthesia, *ibid.* **135**:507, 1932. (f) De Courcy, J. L.: New Methods of Controllable Spinal Anesthesia: The Use of Pitkin's Method in One Hundred Cases, Am. J. Surg. **5**:620, 1928. (g) Pitkin, G. P.: Spinal Anesthesia, in Lewis, Dean: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1935, vol. 1, chap. 5, pp. 22-23. (h) MacRobert, G.: The Cause of Lumbar Puncture Headache, J. A. M. A. **70**:1350 (May 11) 1918.

2. Stillwell, W. C.: Lumbar Anesthesia: Résumé of Seven Hundred and Fifty-One Cases, Minnesota Med. **15**:73, 1932. Anderson, E. R.: Complications of Spinal Anesthesia, Journal-Lancet **51**:73, 1932. Frazier, C. H.: Surgery of the Spine and Spinal Cord, New York, D. Appleton & Company, 1918. Parker, H. L.: Headache Following Diagnostic Spinal Puncture, Proc. Staff Meet., Mayo Clin. (supp. 1) **4**:369, 1929. Evans.^{1b} Heldt.^{1d} Pitkin.^{1e}

3. (a) Harrison, P. W.: Postanesthetic Headache, Arch. Surg. **32**:99 (Jan.) 1936. (b) Babcock, W. W.: Spinal Anesthesia in Fact and Fancy, Surg., Gynec. & Obst. **59**:94, 1934. (c) Braun, H.: Localanesthetie, ed. 3, Leipzig, Johann Ambrosius Barth, 1914. Evans.^{1b}

With a view to obtaining definite information regarding these assertions, we deliberately contaminated the solution made by dissolving procaine hydrochloride in cerebrospinal fluid by the addition of tincture of iodine and a solution of 2, 4, 6-trinitrophenol. We also compared the effects of using procaine hydrochloride dissolved in physiologic solution of sodium chloride, tap water and distilled water with procaine hydrochloride dissolved in cerebrospinal fluid.

METHOD

The experiment was conducted in five parts, twenty-five patients being used in each group. The anesthetic agent used was procaine hydrochloride, in doses

TABLE 1.—Data on Postoperative Headache in Group 1 After Spinal Anesthesia

Case	Date	Age	Operation	Headache
1	4/30	28	Appendectomy.....	None
2	5/10	25	Hernioplasty; appendectomy; resection of ovary.....	None
3	5/11	18	Appendectomy.....	None
4	5/12	37	Appendectomy; suspension of uterus.....	None
5	5/12	45	Appendectomy.....	None
6	5/14	55	Vaginal hysterectomy; perineorrhaphy.....	None
7	5/13	51	Excision of osteoma of foot.....	None
8	5/13	50	Amputation of cervix; interposition; Bell-Beattner operation; perineorrhaphy.....	None
9	5/13	27	Cholecystectomy; appendectomy.....	None
10	5/13	19	Appendectomy; oophorectomy on right.....	None
11	5/14	26	Open reduction for fractured patella.....	None
12	5/14	44	Hernioplasty.....	None
13	5/14	18	Appendectomy; resection of ovary.....	None
14	5/14	31	Hernioplasty.....	None
15	5/14	44	Cholecystectomy; appendectomy; suspension of uterus.....	None
16	5/14	37	Appendectomy.....	None
17	5/15	55	Bilateral hernioplasty.....	None
18	5/15	60	Exploratory operation for carcinoma of rectosigmoid region with metastasis to liver	Preoperative
19	5/16	34	Bilateral hernioplasty.....	None
20	5/16	33	Bilateral hernioplasty; hemorrhoidectomy.....	None
21	5/16	28	Bilateral hernioplasty.....	None
22	5/16	27	Left oophorectomy; appendectomy.....	None
23	5/16	21	Appendectomy.....	None
24	5/17	25	Excision of pilonidal cyst.....	None
25	5/17	32	Appendectomy.....	None

of 150 mg. All the injections were made between the second and the third lumbar vertebra with as nearly the same force and speed as possible, in an attempt to secure uniformity of introduction into the subarachnoid space. The injections were made with the Labat needles (22 gage), which we always use for this type of procedure.⁴ No attempt was made to discriminate between types of headaches or degrees of severity. If any headache was felt, it was recorded.

Group 1.—To 150 mg. of procaine hydrochloride dissolved in 4 cc. of cerebrospinal fluid, 1 minim (0.062 cc.) of tincture of iodine was added, and the resultant mixture was injected into the subarachnoid space. The operation was performed, and headache was awaited. The results are recorded in table 1.

4. Koster, H.: Spinal Anesthesia (with Special Reference to Its Use in Surgery of the Head, Neck and Thorax), *Am. J. Surg.* 5:554, 1928. Koster, H., and Kasman, L. P.: Spinal Anesthesia for the Head, Neck, and Thorax: Its Relation to Respiratory Paralysis, *Surg., Gynec. & Obst.* 49:617, 1929.

The patient in case 18 on whom an exploratory operation was done for carcinoma of the rectosigmoid region, had a preoperative frontal headache for several days. At operation, miliary peritoneal and hepatic metastases were found. Post-operatively the patient continued to complain of frontal headache. Weeks subsequently there developed personality changes, an increase in intracranial pressure and ocular changes, all indicative of cerebral metastasis.

Group 2.—To 150 mg. of procaine hydrochloride dissolved in 4 cc. of cerebrospinal fluid, 1 minim of a solution of trinitrophenol (6 per cent trinitrophenol in 60 per cent alcohol) was added, and the resultant mixture was injected into the subarachnoid space. The operation was then performed, and headache was awaited. The results appear in table 2.

Two patients in this series complained of headache postoperatively.

TABLE 2.—*Data on Postoperative Headache in Group 2 After Spinal Anesthesia*

Case	Date	Age	Operation	Headache
1	5/18	29	Left salpingectomy; appendectomy.....	None
2	5/18	28	Hemorrhoidectomy.....	None
3	5/18	66	Interposition; perineorrhaphy.....	None
4	5/18	13	Appendectomy.....	None
5	5/18	40	Appendectomy; separation of pericholecystic adhesions.....	None
6	5/19	33	Cholecystectomy; sterilization; appendectomy	None
7	5/19	43	Supracervical hysterectomy; appendectomy...	2 days
8	5/19	53	Choledochostomy; cholecystectomy; appendectomy.....	None
9	5/19	39	Supracervical hysterectomy; oophorectomy; appendectomy.....	None
10	5/19	32	Supracervical hysterectomy; left oophorectomy.....	None
11	5/19	43	Supracervical hysterectomy; oophorectomy...	None
12	5/19	24	Hernioplasty; appendectomy.....	None
13	5/19	16	Appendectomy.....	None
14	5/19	51	Panhysterectomy; appendectomy.....	None
15	5/19	35	Cholecystectomy; appendectomy; sterilization.....	3 days
16	5/20	36	Appendectomy.....	None
17	5/20	44	Supracervical hysterectomy; oophorectomy; appendectomy.....	None
18	5/20	53	Hemorrhoidectomy.....	None
19	5/20	24	Appendectomy.....	None
20	5/20	24	Appendectomy; resection of ovary.....	None
21	5/21	11	Appendectomy.....	None
22	5/21	35	Cholecystectomy; appendectomy.....	None
23	5/23	39	Cholecystectomy; appendectomy.....	None
24	5/22	36	Hernioplasty.....	None
25	5/22	17	Appendectomy.....	None

Group 3.—One hundred and fifty milligrams of procaine hydrochloride was dissolved in 4 cc. of sterile physiologic solution of sodium chloride, and the resultant mixture was injected into the subarachnoid space after 4 cc. of cerebrospinal fluid was withdrawn. The results as regards postoperative headache are shown in table 3.

Only one patient in this group complained of headache postoperatively.

Group 4.—One hundred and fifty milligrams of procaine hydrochloride was dissolved in 4 cc. of sterile tap water, and the resultant mixture was injected subarachnoidally after 4 cc. of cerebrospinal fluid was withdrawn. The results as regards headache are shown in table 4.

Two patients in this group had headache postoperatively.

TABLE 3.—Data on Postoperative Headache in Group 3 After Spinal Anesthesia

Case	Date	Age	Operation	Headache
1	6/ 4	19	Appendectomy.....	None
2	6/ 4	47	Hernioplasty.....	None
3	6/ 5	35	Cholecystectomy; appendectomy.....	None
4	6/ 5	48	Supravaginal hysterectomy.....	1 day
5	6/ 8	42	Thyroidectomy.....	None
6	6/ 6	29	Cauterization of cervix; tracheloplasty.....	None
7	6/ 8	26	Closure of gastrocolic fistula.....	None
8	6/ 6	13	Appendectomy; resection of ovary.....	None
9	6/ 7	45	Supracervical hysterectomy; appendectomy...	None
10	6/ 7	16½	Appendectomy.....	None
11	6/ 7	25	Appendectomy.....	None
12	6/ 8	53	Perineorrhaphy; Kelly's plication of urethra..	None
13	6/ 8	18	Appendectomy.....	None
14	6/ 8	35	Perineorrhaphy; myomectomy; oophorec- tomy; appendectomy; hemorrhoidectomy...	None
15	6/ 8	25	Appendectomy.....	None
16	6/ 9	33	Repair of anterior and posterior wall; supra- cervical hysterectomy.....	None
17	6/ 9	57	Appendectomy.....	None
18	6/10	21	Salpingectomy for ectopic pregnancy; appen- dectomy.....	None
19	6/10	57	Vaginal hysterectomy; perineorrhaphy.....	None
20	6/11	32	Left salpingo-oophorectomy; appendectomy; suspension of uterus.....	None
21	6/11	27	Cholecystectomy; appendectomy.....	None
22	6/11	20	Appendectomy.....	None
23	6/11	32	Supracervical hysterectomy; oophorectomy; appendectomy.....	None
24	6/11	32	Appendectomy.....	None
25	6/11	16	Appendectomy.....	None

TABLE 4.—Data on Postoperative Headache in Group 4 After Spinal Anesthesia

Case	Date	Age	Operation	Headache
1	5/26	58	Splenectomy.....	None
2	5/26	61	Gastrectomy; Murphy's button gastro-jeju- nostomy.....	None
3	5/26	29	Hernioplasty.....	None
4	5/26	36	Left oophorectomy.....	2 days
5	5/23	20	Bilateral hernioplasty.....	None
6	5/26	25	Myomectomy suspension; oophorectomy.....	2 days
7	5/26	43	Perineorrhaphy.....	None
8	5/27	46	Supracervical hysterectomy; appendectomy...	None
9	5/26	11	Appendectomy.....	None
10	5/27	34	Supracervical hysterectomy; cholecystectomy; appendectomy; oophorectomy.....	None
11	5/26	42	Appendectomy.....	None
12	5/29	33	Hernioplasty; appendectomy.....	None
13	5/29	35	Hernioplasty; appendectomy.....	None
14	5/29	30	Bilateral oophorectomy; appendectomy.....	None
15	5/29	29	Appendectomy.....	None
16	5/29	41	Excision of pilonidal cyst.....	None
17	5/29	36	Hernioplasty (Gallie's).....	None
18	5/30	59	Hernioplasty, incarcerated femoral.....	None
19	5/31	35	Bilateral oophorectomy; appendectomy.....	None
20	6/ 2	22	Hernioplasty, scrotal.....	None
21	6/ 2	62	Hernioplasty, scrotal.....	None
22	6/ 2	4½	Hernioplasty, inguinal.....	None
23	6/ 2	30	Appendectomy.....	None
24	6/ 3	30	Diagnostic curettage for carcinoma of uterus	None
25	6/ 3	47	Supracervical hysterectomy; oophorectomy; hemorrhoidectomy.....	None

Group 5.—One hundred and fifty milligrams of procaine hydrochloride was dissolved in 4 cc. of distilled water, and the resultant mixture was injected sub-arachnoidally after 4 cc. of cerebrospinal fluid was withdrawn. The results as regards postoperative headache are shown in table 5.

TABLE 5.—*Data on Postoperative Headache in Group 5 After Spinal Anesthesia*

Case	Date	Age	Operation	Headache
1	7/13	57	Separation of adhesions.....	None
2	7/13	50	Supracervical hysterectomy; appendectomy...	None
3	7/13	25	Appendectomy; hemorrhoidectomy.....	None
4	7/13	37	Appendectomy.....	None
5	7/13	11	Appendectomy.....	None
6	7/13	24	Appendectomy.....	None
7	7/14	37	Appendectomy; sterilization; myomectomy...	None
8	7/13	19	Appendectomy.....	None
9	7/14	47	Hernioplasty.....	None
10	7/14	66	Resection of sigmoid colon.....	None
11	7/15	60	Exploratory; biopsy.....	None
12	7/16	36	Exploratory; appendectomy.....	None
13	7/15	34	Supracervical hysterectomy; right oophorectomy; appendectomy.....	None
14	7/14	15	Appendectomy.....	None
15	7/15	21	Appendectomy; resection of ovary.....	None
16	7/16	65	Hernioplasty.....	None
17	7/16	40	Supracervical; hysterectomy; oophorectomy; appendectomy.....	None
18	7/15	19	Appendectomy.....	None
19	7/15	45	Appendectomy.....	None
20	7/15	54	Resection of intestine (ileitis)...	None
21	7/16	21	Repair of hydrocele.....	None
22	7/16	26	Appendectomy.....	None
23	7/17	27	Appendectomy.....	None
24	7/17	54	Excision of varicosities.....	None
25	7/18	36	Appendectomy; myomectomy; sterilization; perineorrhaphy; biopsy of intestine.....	None

COMMENT

In an editorial by one of us⁵ concerning the criteria of scientific proof, the point was made that uncontrolled biologic phenomena could not be used as significant data unless the material represented large values numerically. Thus it was shown that in our clinic, where spinal anesthesia was used as a routine for all major operations, as many as a hundred consecutive patients would frequently be anesthetized in this manner without a single instance of postoperative headache occurring, and then without any recognizable departure from the routine previously used, four or five subsequent patients would have headache. With one of these groups of one hundred headache-free patients as the criterion, it could have been said that the technic employed obviated the occurrence of postoperative headache. These next four or five patients would have

5. Koster, H.: Evaluation of the Results of Treatment, *Am. J. Surg.* 20: 157, 1933.

demonstrated how erroneous the conclusion was. In a controlled series, however, in which individual factors are tested, comparatively small numbers can give significant results.

It seems hardly likely that contamination of injected fluid with iodine could produce postoperative headache. Iodine precipitates procaine hydrochloride, and this reaction is the basis for one of the chemical tests for procaine hydrochloride. Therefore, the iodine itself could not act as an irritant. If the insoluble compound formed by iodine and procaine hydrochloride is the irritating factor, then it must be very potent, since the amount of iodine which could be carried by the tip of the needle from dripping skin through approximately 3 inches (7 cm.) of tissues before the arachnoid is reached must be very small—certainly a minute fraction of a minim. The failure to produce headache uniformly in the twenty-five cases in which the solution of procaine hydrochloride was deliberately contaminated with 1 minim of tincture of iodine suggests strongly that contamination with iodine is not a potent factor in the development of postoperative headache after spinal anesthesia.

In our clinic, where spinal anesthesia has been induced in approximately 11,000 instances in the past eleven years, a solution of 6 per cent trinitrophenol in 60 per cent alcohol has been used for preparation of the skin. If contamination by solutions used for this preparation is responsible for headache, then in our cases it must have been either the trinitrophenol or the alcohol which was the contaminant. However, the failure to produce headache uniformly in the twenty-five cases in which one minim of solution of trinitrophenol was deliberately added to the anesthetic agent injected again suggests strongly that it is not a causal agent.

The relation of hypertonicity to the development of postoperative headache has never been demonstrated. The experiments with saline solution and water as solvents for procaine hydrochloride have failed to yield any significant information, and it must be conceded that from the data it cannot be concluded that postoperative headache depends on the hypertonicity or the hypotonicity of the injected solution.

No reliable data concerning the effect of varying the p_H on the development of postoperative headache are available. The p_H of cerebrospinal fluid plus procaine hydrochloride is 7; that of tap water and procaine hydrochloride is 5.93, and that of distilled water plus procaine hydrochloride is 5.63. After the injection of procaine hydrochloride dissolved in distilled water, headache was not uniformly produced. However, that is not surprising when it is remembered that only 4 cc. of the procaine hydrochloride solution is injected into a fluid the minimum amount of which is at least 50 cc. and which contains

6. The p_H determinations were made with a glass electrode.

considerable buffer substance. As a matter of fact, if three minutes after the injection of 4 cc. of distilled water containing 150 mg. of procaine hydrochloride into the subarachnoid space a sample of cerebrospinal fluid is withdrawn, it is found to have a p_H of 7.

It can be seen from the tables that if the one patient in group 1 who had a headache preoperatively is left out of the consideration, there were five patients with postoperative headache among the one hundred who were used in the experiments. The ordinary incidence of postoperative headache in our experience is 5 per cent.

The experiments were carried out on the first four groups of patients consecutively. There was an interval between the experiments on group 4 and group 5, during which time one hundred and thirty-five persons were anesthetized with procaine hydrochloride dissolved in cerebrospinal fluid. Of this number, not a single person had headaches postoperatively.

CONCLUSIONS

1. The addition of either tincture of iodine or a solution of trinitrophenol to procaine hydrochloride dissolved in cerebrospinal fluid does not add to the risk of development of headache postoperatively.

2. Hypotonicity or hypertonicity as occasioned by using tap water, saline solution or distilled water also is not a factor in the production of headache postoperatively.

3. Buffer substances are present in cerebrospinal fluid in sufficient quantities to render innocuous ordinary solutions used to develop anesthesia which might have a p_H as low as 5.63.

INTESTINAL OBSTRUCTION

AN ATTEMPT AT AN IMPROVED DISCUSSION OF ITS PATHOLOGIC
PHYSIOLOGY AND TREATMENT BASED ON A SIMPLE
CLASSIFICATION AND ON PAST EXPERIMENTAL
AND CLINICAL EXPERIENCE

J. K. DONALDSON, M.D.

Associate Professor of Surgery, University of Arkansas Medical School.
LITTLE ROCK, ARK.

In 1933, in conjunction with Dr. B. F. Stout, I initiated some experiments on intestinal obstruction. Since that time continued experimental and clinical work on this problem have contributed toward a conception of this disease which is more comprehensive and proper than the conception we previously held.

We have been encouraged by others to believe that certain phases of our previous work, which will be discussed briefly later in this paper, may have been of some value in clarifying somewhat one fundamental aspect of the condition.¹ I venture to present here a simplified classification of intestinal obstruction which I feel is amenable to a comprehensive, yet brief and improved, discussion of its known pathologic physiology. The majority of the points mentioned have been previously reviewed by others. Certain aspects of the classification and discussion, however, have not.

It must be admitted that a perfect classification of any disease is impossible as long as there are unsolved aspects of it, and certainly there is more to be learned about obstruction. The importance of an impaired blood supply in cases of obstruction has not been as widely appreciated as it should have been because of the confusion attending the many theories and discussions which have been carried on over the world regarding unknown aspects of obstruction. In accepting the importance of the impaired blood supply as I do in the following discussion, I do so on the basis of the work of Kader, Murphy and Vincent, Gatch, Gatch and Culbertson, McIver, Wilkie and many others. The importance of this factor has been proved beyond question. It must be acknowledged that investigators do not know the exact mechanism of the deleterious action of an impaired blood supply. It

From the Department of Surgery, University of Arkansas Medical School.

1. Donaldson, J. K., and Stout, B. F.: Mesenteric Thrombosis: Arterial and Venous Types as Separate Clinical Entities, *Am. J. Surg.* 29:208 (Aug.) 1935.

may, furthermore, be acknowledged that there may be some legitimate dispute as to the primary importance of neurogenic and other factors in distention associated with obstruction. From a practical standpoint, however, one is justified in accepting any hypothesis as a working basis as long as this hypothesis procures end-results which are as good as, or superior to, any other end-results. The following trend of thought will at present procure these results.

In accepting the theory that distention may produce sufficient ischemia of the mucous membrane of the intestine to cause a lethal absorption of toxin, one accepts dogma which has good support. Gatch and Culbertson² are the latest workers to offer evidence in this direction. It probably would be unfair to say that other influences never play a part in distention. It seems probable, however, that when distention is

*Classification of Intestinal Obstruction**

I Direct Obstruction of the Lumen		II Indirect Obstruction of the Lumen	
1. With primary interference with blood supply	2. Without primary interference with blood supply	1. With primary interference with blood supply	2. Without primary interference with blood supply
a (a) Folded strangulated loop in cavity	a (c) Simple high or low obstruction with no folded loop	a (e) Occlusion of mesenteric arteries without direct obstruction of lumen	a (g) Postoperative ileus
b (b) Strangulated loop isolated from cavity, as in incarcerated hernia	b (d) High or low obstruction with added obstruction of folded loop	b (f) Occlusion of mesenteric veins without direct obstruction of lumen	b (h) Ileus from acute infectious disease or from other causes without direct obstruction of lumen

* It is to be acknowledged, of course, that for academic completeness subclassifications dealing with the wide variety of specific causes of obstruction should be added to this classification. These details of subclassification, however, should not be confused with the fundamentals of pathologic physiology with which the classification given here deals.

the cause of death, as it sometimes is, it is always sufficiently marked to interfere with the blood supply to the mucous membrane, even though other factors may possibly enter into the picture. As far as present day knowledge is concerned, however, the proper treatment is the same whether or not one chooses to accept the factor of an impaired blood supply in distention as one of the main factors in the morbid picture.

THE TWO CHIEF CONCERNS IN OBSTRUCTION

Before referring to the classification in the table, I am assuming, then, with the possible reservations mentioned previously, that in practically all cases of obstruction there are two main problems. 1. The first one is the potential loss of fluid and salts. The seriousness of this factor is widely appreciated and needs no further consideration for the moment. 2. The second is potential interference with the blood supply to the

2. Gatch, W., and Culbertson, C. G.: Circulatory Disturbances Caused by Intestinal Obstruction, *Ann. Surg.* **102**:619 (Oct.) 1935.

intestine, either by primary interference or by interference secondary to distention. The physiologic relationship of other factors to these two highly important ones will be discussed later.

The classification of intestinal obstruction appears in the accompanying table.

It may be noted that all types of obstruction are divided into two large classes: (I) that in which there is an actual direct blockage of the lumen of the intestine, such as may rise, for example, from an adhesion or from an intra-intestinal or extra-intestinal foreign body or tumor, and (II) that in which the lumen of the intestine is indirectly obstructed but not closed, as in postoperative ileus. These two main divisions are further divided into two groups on the basis of one of the two chief concerns in obstruction, namely, the blood supply: (1) that group in which the blood supply is primarily interfered with and (2) that in which the blood supply is not primarily interfered with but in which it may be secondarily threatened by distention. On the simple foundation of these parts of the classification, one can rapidly build an understanding of diagnostic and therapeutic considerations. Before proceeding, however, with further discussion of the relation of secondary factors a brief consideration of certain differences caused by strangulation of the arterial supply as against an uncomplicated strangulation of the venous return from the intestine should be given.

NECESSITY FOR APPRECIATING THE DIFFERENCE BETWEEN ARTERIAL AND VENOUS MESENTERIC OCCLUSION

The differences between pure venous mesenteric occlusion and arterial mesenteric occlusion have a bearing on the fundamental physiology of obstruction as a whole. Previous to 1934 or 1935 it seemed to have been generally accepted that the end-results of occlusion of the mesenteric veins and those of occlusion of the mesenteric arteries were the same. Mention had been made of the anatomic difference of the two types, but a full realization of the pathologic differences between the two had never, as far as I know, been appreciated previous to the work of Dr. Stout and myself on this subject.³ The opinions expressed in our published reports have been confirmed or at least upheld by others since that time. Ochsner has referred to clinical cases of purely venous thrombosis of the mesenteric vessels in which recovery occurred without resection. Certain parts of the work done by Knight and Slome⁴ evidently gave results similar to ours.

3. Donaldson, J. K., and Stout, B. F.: Mechanics of Absorption in Intestinal Obstruction, *Texas State J. Med.* **30**:455 (Nov.) 1934. Donaldson and Stout.¹

4. Knight, G. C., and Slome, D.: Intestinal Strangulation, *Brit. J. Surg.* **23**:821, 1936.

Held and Goldbloom⁵ reported a case of venous thrombosis of the mesenteric vessels following repeated administration of phenolphthalein. So it seems an established fact that there are vast pathologic and clinical differences between pure venous occlusion of the mesenteric vessels and pure arterial occlusion, provided the lumen of the intestine remains sufficiently unobstructed in the former. Occlusion of some of the mesenteric veins does not always cause secondary arterial thrombosis; it does not necessarily cause gangrene of intestinal tissue if the intestinal lumen remains sufficiently patent to empty the involved loop of collecting fluids, and it does not per se cause paralytic ileus; it does give rise to a different clinical picture than that produced by arterial occlusion. Failure to realize these facts has been responsible for some misinterpretation of the problem of obstruction. For example, statements of good surgeons have depreciated to a certain extent the danger of gangrenous intestine, cases being cited in which, after resection of a loop of blackened intestine which had evidently been present for days, the patient recovered. Likewise, it has been said that the omentum and the peritoneum will often wall off a gangrenous loop of intestine in the peritoneal cavity, thereby decreasing the danger. The latter mechanism and result may take place in a case of incarcerated hernia, but the tremendous fulminating danger of gangrene should never be minimized. Unquestionably confusion of the loops of blackened but not gangrenous intestine which occur in cases of venous occlusion with truly gangrenous loops in cases of arterial occlusion has been responsible for some misunderstanding. I have often seen experimentally a blackened intestinal loop in a case of purely venous occlusion which "walled off," with resulting clinical recovery, but I have never seen true gangrene of the intestine in an animal or in man go through a similar process to successful recovery. Such an incident, if it occurs at all, must be extremely rare.

MECHANISM OF THE SECONDARY FACTORS

The mechanism of the secondary factors of intestinal obstruction, as outlined in the table, are discussed briefly.

a (c). In the simple type of obstruction in which no direct interference with the blood supply is present, what is the mechanism of the developing pathologic process? If the obstruction is high it is generally known that vomiting with loss of fluid and salts rapidly supervenes and may be the most important part of the picture. Distention may not develop, because the unobstructed intestine may automatically regurgitate through the pylorus. Consequently, interference with the

5. Held, I. W., and Goldbloom, A. A.: Three Rare Intra-Abdominal Cases, *S. Clin. North America* 14:389 (April) 1934.

blood supply may not occur.⁶ In this type of obstruction infusions of saline solution, combined with decompression by the use of the Wangenstein or nasal catheter if distention is present, will give immediate temporary relief. Obstruction has righted itself after such treatment. Temporization carries, however, the responsibility of assuming surety as to type of obstruction.

If the simple obstruction is lower in the small bowel, serious vomiting will develop later. Distention of the intestine will appear, eventually interfering with the blood supply to the mucous membrane. Distention will be harder to control by decompression through the nasal catheter because of the loops of intestine folding on themselves.

If the simple obstruction is in the large bowel, vomiting will become a serious factor only late in the disease, if ever. Distention in the large bowel may not cause the production or absorption of toxin directly but may cause a rupture of an ischemic area in the cecum, even before serious subjective symptoms have presented.⁷

b (d). If the obstruction is of the looped type in which the bowel is folded on itself, obstructing a segment as well as the main continuity of the intestine, there is immediately superimposed on the consideration as to the level of obstruction the added factor of the obstructed loop. This loop may rapidly become distended, bringing ischemia to its mucous membrane or additional constriction to its primary blood supply. Temporization procedures in this type are extremely dangerous.

a (a). If one has a gangrenous loop of intestine free in the peritoneal cavity anywhere, its level is of secondary consequence. Unless the area of gangrene is removed promptly from the cavity, death will follow. With a folded loop, however, in which there is interference with the blood supply, one should realize the different pathologic pictures which may be produced by purely venous occlusion as against arterial occlusion. As previously stated, every blackened intestinal loop is not gangrenous. Also, there is a difference between the advancing pathologic condition in a folded loop to which the venous apparatus and the lumen are both occluded and that of an intestine in which the veins supplying it are closed with the intestine not occluded. In the former the collection of fluid and distention of the intestine are rapid, with

6. Jenkins, H. P., and Beswick, W. F.: Prolongation of Life for Seventy Days in High Intestinal Obstruction by Administration of Sodium Chloride and Nutritive Material Below the Site of Occlusion, *Arch. Surg.* **26**:407 (March) 1933.

7. Saeltzer, D. V., and Rhodes, G. K.: Diastasic Perforation of the Normal Cecum, *Ann. Surg.* **101**:1257 (May) 1935.

tremendous bacterial proliferation and interference with the arterial supply soon presenting.

b (b). If a strangulated loop is isolated within an incarcerated hernia so tightly that no absorption through the mesentery or peritoneal cavity can occur, it is for the moment, to an extent, a simple obstruction. In operating for this type of obstruction one should be extremely careful when gangrenous intestine is freed from the incarceration to prevent its toxic content from moving into the lumen of the intestine remaining in the peritoneal cavity, if the latter bowel is damaged at all by distention. Otherwise a severe dose of toxin may be absorbed.

a (c). In obstruction occurring from paralysis secondary to arterial mesenteric occlusion in which no direct obstruction of the lumen is present, one is, as with gangrenous intestine of other types, concerned only with immediate operation.

b (f). If the occlusion of the vessels is purely of the venous type without obstruction of the lumen, the clinical course which has been described by Dr. Stout and myself ¹ may possibly end in recovery if the involvement of the intestine is not too extensive. Prompt surgical intervention, however, is probably, as a rule, the treatment of choice.

a (g) and *b (h).* In the last two groups, in which a primary paralytic ileus is present, as for example in acute infectious diseases or in the primarily paralytic postoperative type, abdominal exploration is not indicated. Other decompression measures may be life saving.

The differential diagnosis of the foregoing types of obstruction will not be discussed here. There are points of difference between all types. It can readily be seen how complicated the differential picture between many of them usually would be, however, if the diagnosis were to be made early and with surety. Furthermore, general statistics reveal that operation for simple obstruction within twenty-four hours after the onset produces a low mortality. The mortality is still lower if operation is done earlier. For the gangrenous types, as previously stated, the most prompt surgical intervention possible is essential. Absorption of toxin probably starts within thirty minutes after the blood supply is strangulated.⁴ If operation is delayed more than twelve hours after the onset of gangrene, a very high death rate is to be expected. I know of no mortality statistics which subdivide the twelve hour period in reference to gangrene, but I feel that with every single hour's delay after gangrene supervenes the mortality is increased.

So when one keeps in mind the different pathologic pictures of obstruction, the difficulty of an early clinical differentiation between most of them and the mortality statistics as related to early operation in most types of the disease, it is easy to understand the grave

responsibility one assumes when one uses temporization measures to postpone operation in all but the primary paralytic types, as listed in *a (g)* and *a (h)* or sometimes in *b (f)* of the classification. Fortunately, these types are fairly easily differentiated from the others.

SUMMARY

A discussion of the pathologic physiology and treatment of intestinal obstruction as based on a simple classification is presented. The majority of the points in this discussion have been previously mentioned, but certain aspects of it are offered as an improvement over some conceptions formerly held.

Previous experimental and clinical work citing differences in the pathologic picture of the arterial and of venous types of mesenteric occlusion are discussed. These differences as they are related to certain fundamentals of the problem of obstruction as a whole should be more fully appreciated.

A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.

LOS ANGELES

FRANK HINMAN, M.D.

SAN FRANCISCO

ALEXANDER VON LICHTENBERG, M.D.

BUDAPEST, HUNGARY

ALEXANDER B. HEPLER, M.D.

SEATTLE

ROBERT GUTIERREZ, M.D.

NEW YORK

GERSHOM J. THOMPSON, M.D.

AND

JAMES T. PRIESTLEY, M.D.

ROCHESTER, MINN.

AND

VINCENT J. O'CONOR, M.D.

CHICAGO

KIDNEY

Anomalies.—Shih and Char¹ stated that congenital solitary kidney may be defined as an anomalous condition in which one kidney is absent because of a disturbance of growth of the nephrogenic tissue in embryonic life and the existing kidney has developed from one renal bud. If the solitary kidney is healthy, congenital absence of the opposite kidney does not give rise to pathognomonic symptoms, and the condition may exist for years without the patient being aware of it.

It cannot be overemphasized that recognition of solitary kidney is of paramount importance and should merit the great concern of the urologic surgeon. A congenital solitary kidney is compatible with normal physiologic function, and a patient with this anomaly maintains full working capacity. The condition is of clinical significance only in the presence of renal disease.

Operation should be recommended only when it is absolutely imperative, and surgical procedures should be as conservative as possible. Experience has demonstrated that the risk of operation on the solitary kidney varies directly with the impairment of function and the degree

1. Shih, H. E., and Char, G. Y.: Congenital Solitary Kidney, Chinese M. J. 50:821-826 (June) 1936.

of infection and that delay in operating on a solitary kidney until urinary obstruction or anuria has developed definitely increases the operative mortality. In the presence of good renal function and in the absence of infection, a great variety of surgical procedures have been and may be performed on the solitary kidney, with gratifying results.

This anomaly is of interest from the standpoint of its genesis and of importance because of its significance to the patient. This condition, even though it is infrequent, should be kept in mind by all those who are interested in surgical treatment of renal conditions.

Char, Shih and Wen² reported 14 cases of duplication of the kidney and ureter. The pathologic picture, symptomatology, diagnosis, prognosis and treatment were considered. The authors pointed out that the complicating pathologic lesion may be found in either the ectopic or the normal segment of the kidney, in spite of the general belief that the upper ectopic segment is usually the seat of disease. From clinical and embryologic studies, it is concluded that as long as proper connections exist between the supernumerary kidney and its ureter it is capable of the functions of a normal organ. Their findings tend to endorse the view that these anomalies develop as a result of a separate out-budding from the mesonephric duct or as a bifurcation of the original ureteral bud.

Mayers³ stated that congenital displacement is to be distinguished from acquired displacement of the kidney. Marked displacement of congenital origin is uncommon. One of the rarest types is a condition in which both kidneys are on the same side of the body. There is a similarity between various forms of displacements and anomalies of structure which often causes confusion in the terminology; for example, a horseshoe kidney which is situated entirely on one side of the midline is identical with a fused type of crossed renal ectopia.

The embryologic factors involved were considered. There are two chief schools of thought: (1) that which believes displacement is due to failure of ascent of the kidney and (2) that which believes that it is attributable to descent of the kidney. Both schools believe that the mechanism involved is closely related to the process of vascularization and that other related factors are variations in the location and branching of the ureteral bud. The marked forms of displacement occur early in embryonic life.

The fused type of crossed renal ectopia is perhaps ten times more frequent than the unfused type. A search of the literature revealed reports of 19 cases which were in all probability true cases, or cases of

2. Char, G. Y.; Shih, H. E., and Wen, I. C.: Duplication of the Kidney and Ureter, *J. Urol.* **36**:305-326 (Oct.) 1936.

3. Mayers, M. M.: Crossed Renal Ectopia, *J. Urol.* **36**:111-122 (Aug.) 1936.

the unfused type, of crossed renal ectopia. Undoubtedly many other cases which have been reported in the literature as of the fused type may be of the unfused type. Mayers reported 7 such cases.

Nineteen cases of crossed renal ectopia, not including the 7 reported by Mayers, presented the following characteristics: In 8, the patients were women, and in 10, men; in 1 case the sex was not reported. The right kidney was involved in 3 cases, the left in 15 cases and both in 1 case. The crossed kidney was under the uncrossed kidney in 17 cases and over the uncrossed kidney in 1 case. In 1 case both kidneys were crossed.

Mayers added to those reported in the literature 1 case in which the condition bore all the characteristics of an unfused type of crossed renal ectopia. The patient was a man whose right kidney was uncrossed and whose left kidney was crossed over and placed under the right. There was pyelitis of both kidneys, and the right kidney contained three large calculi. Diagnosis was made by examination and confirmed at operation. This case is unique as calculi were present in the uncrossed partner of the combination. As far as Mayers could determine, there is no other case reported in the literature in which this situation exists.

Lower⁴ described a case of fused kidney in which three almost distinct kidneys had fused into one mass; two of these were in essentially normal position and were joined together by a third kidney lying medially and horizontally in front of the spinal column. This third kidney had a complete pelvis and a ureter, which anastomosed with the ureter of the left kidney at about its middle third. This median supernumerary kidney, which thus constituted the isthmus of a horseshoe kidney fused at the top, was removed with its anomalous ureter, leaving the patient with a right and a left kidney, both of which were functioning well, as was revealed by a postoperative intravenous urogram.

The author, who has had a series of 23 cases of fused kidney, pointed out that extreme care must be taken in establishing the diagnosis in such cases, because the symptoms are so largely referable to the gastro-intestinal tract as to be misleading. Many erroneous diagnoses of acute or chronic appendicitis, gallstones, duodenal ulcer, chronic ulcerative colitis and tumor of the colon have been made by practitioners who did not think of the possibility of horseshoe kidney and hence did not employ urography and the complete laboratory facilities to clear up the diagnosis.

The cardinal symptoms of horseshoe kidney, as summed up by Gutierrez, are umbilical or epigastric pain, extending to the lumbar

4. Lower, W. E.: The Problem of the Fused Kidney, *J. Urol.* **35**:588-595 (June) 1936.

region, chronic constipation and perhaps other gastro-intestinal disorders, and urinary disturbances associated with early signs of nephritis. These symptoms are attributable to the pressure exerted by the horseshoe kidney lying across the spine and close to the great abdominal vessels, the solar plexus and the abdominal sympathetic and parasympathetic nerves.

A complete history should be taken with special reference to subjective as well as to objective symptoms. A tumor situated in the midline may be palpable and is often tender, and pain produced on bending backward sometimes will suggest the presence of a horseshoe kidney. Laboratory studies of the blood and urine should be made. A roentgenographic examination is essential, and this may give the first indication that a horseshoe kidney is present. The important points in establishing a diagnosis from roentgenograms are the outline and position of the kidney, the possible delineation of the isthmus, abnormalities in the shape and contour of the pelvis and calices (the lowermost calices usually point inward toward the midline), the abnormal position of the ureters, which in the horseshoe kidney usually enter the lateral and not the internal aspect of the renal organ, and, finally, any shortening of the ureters, stricture or kinking. The diagnosis is made easier if the kidney contains stones, since if multiple wedge-shaped calculi are present the direction of the axis of the kidney can often be determined from the way the stones are placed.

When symptoms are so severe that the patient seeks aid, an indwelling catheter should be inserted at once to secure drainage and to relieve infection; rest in bed, administration of urinary antiseptics and cathartics and intravenous injection of physiologic solution of sodium chloride should also be employed. Permanent cure can be obtained, however, only by surgical intervention, consisting of division of the isthmus with or without nephropexy, according to the degree of motility of the kidneys.

Ptoxis.—Gouverneur and Cachin⁵ stated that most of the poor results from operations on movable kidneys in the past have been caused by a failure to recognize the correct indications. The mere presence of a movable kidney, with pain, was enough to invite operation, without any inquiry about the morphologic condition of the pelvis, ureter and kidney or the amount of infection in the urinary tract. The authors insisted on the paramount importance of taking retrograde ureteropyelograms with the patient in the vertical position and of taking into consideration the site of the pain, which shows the true position of the kidney, the form of the pelvis and, especially, the topography of kinks of the ureter.

5. Gouverneur, R., and Cachin, Charles: Le traitement chirurgical des ptoses rénales: Indications; technique; résultats, J. de chir. 47:754-770 (May) 1936.

They have operated on 28 patients with movable kidney associated with marked functional troubles. The results, both anatomic and functional, were always excellent. In all but 5 cases retrograde ureteropyelograms were taken, the intravenous method of urography being used. It requires more delicate judgment to recognize the indications for operation than to perform the operation, for the technic is very simple. The patient should be studied for some time before the operation, as there is no need for hurry; several examinations should always be made. One should not operate on a patient with several other operative scars, for renal ptosis may be only the most apparent element of some general disease. Mild pyelonephritis in a ptotic kidney is an indication for operation; when a long course of treatment does not result in improvement, operation is indicated, and if the condition is a frank pyelonephritis, this is all the more true. Pyuria, which is not too excessive, is another indication for operation. If hydronephrosis is present, one must make sure that this is secondary to the ptosis and not a congenital condition, for in the latter case reposition will do no good.

At operation, the authors advocated high reposition. Despite some opinions to the contrary, their films revealed good results from this method. The old technics of Guyon and Albarran are inadequate, and yet they are the ones most frequently used. The incision used by Gouverneur and Cachin is slightly different from the usual lumbotomy; it is shorter, commences a little above and internal to the anterosuperior iliac spine and goes obliquely toward the costolumbar angle; two finger-breadths below this it becomes vertical and continues directly upward to the tenth rib. It is only during the course of the operation that the situation of the kidney can be learned exactly, for it depends on the morphologic relations of the ribs, the thorax and the bed of the kidney. In effecting fixation, the linen threads are drawn from below upward and from within outward through the diaphragm, the two leaflets of the diaphragmatic pleura and the intercostal pleura and the intercostal muscles. A fault to avoid is that of passing the threads which have gone through the intercostal space and the diaphragm outward from the kidney bed; this can easily happen and will result in allowing the kidney to come only partially upward; the left hand placed under the cupola must serve as a guide to the needle. The sutures are tied two and two, the anterior together and the posterior similarly; the assistant in the meantime pushes the kidney into its bed and supports the lower pole. A small suspensory hammock is made for the lower pole of the perirenal fat and the lower part of the renal fascia and is tied above the twelfth rib or sometimes even above the eleventh rib. The patient should be kept in bed for three weeks, after which a course of exercises should be prescribed to strengthen the abdominal muscles.

Smith, McKim and Rush⁶ reported their findings after a study of 238 nephropexies performed on 204 patients in the fourteen years prior to 1934.

They stated that there are four factors in ptosis of the kidney that may be of importance in the production of symptoms: 1. Tension on, and torsion of, the renal pedicle usually causes a sensation of heaviness and weight in the side affected and frequently interferes with the return flow of blood through the renal vein to such an extent as to produce attacks of renal colic in patients in whom there may be no evidence of renal stasis.

2. The excessive stimulation of the sympathetic nerves as a result of the constant pull on the splanchnic area may manifest itself in many ways and probably plays a rather important rôle in the production of the symptoms of the dyspepsia so frequently found in these cases. The frequency of intense headaches and of pain that is referred to a point midway between the scapulae also may result from this excessive stimulation. The so-called "neurasthenia" so commonly found in cases of neglected ptosis of the kidney is undoubtedly caused by excessive stimulation of the sympathetic nerves.

3. The sagging of the midportion of the duodenum can be demonstrated easily by fluoroscopic examination of the gastro-intestinal tract, particularly if this is made with the patient standing and in conjunction with retrograde pyelography.

4. The frequency with which ureteral kinks are demonstrated in cases of ptosis of the kidney is probably quite misleading. It is felt that these kinks are not of any particular clinical importance unless there is evidence of renal stasis or of chronic infection of the renal pelvis.

Two types of altered renal mobility are recognized: the asymptomatic and the symptomatic. The latter type comprised at least 60 per cent of all the authors' cases. They have chosen as a basis for discussion a classification of the latter group based entirely on symptomatology, although the extent of alteration in mobility in each of these groups is rather constant.

The cases are classed in four groups: Those in group 1 are characterized by attacks of acute excruciating pain, simulating renal colic, and the other symptoms of renal ptosis are seldom present. This type of pain is found almost as frequently on the left as on the right side. Often the patient can date the onset of his symptoms from the time of some unusual physical exertion or an accident. The cases in group 2 are characterized by marked gastro-intestinal symptoms suggesting pyloric

6. Smith, P. G.; McKim, G. F., and Rush, T. W.: Nephropexy for Disabilities Due to Abnormal Renal Mobility, *Ann. Surg.* **103**:924-934 (June) 1936.

or duodenal obstruction. Occasionally these are so severe that they have been the cause of a previous operation, such as appendectomy or cholecystectomy. Those in group 3 are characterized by occasional attacks of rather severe renal colic and a marked tendency toward a recurrent pyelitis and hematuria. Symptoms of chronic dyspepsia are usually present. There is in these cases a definite tendency toward neurasthenia. Examination reveals the kidney to have a movement of from $1\frac{1}{2}$ to 3 inches (3.57 to 7.6 cm.) and frequently gives evidence of urinary stasis. It is in this group, which comprised 48 per cent of their series, that the authors had the most uniformly satisfactory results. The cases in group 4 are characterized by more or less constant heaviness and dragging in the side, and usually symptoms suggestive of chronic renal infection are present. If these symptoms are on the right side, symptoms of mild, chronic dyspepsia are usually present also. Examination reveals a very low-lying kidney and usually a dilated and infected renal pelvis.

The vast majority of unsatisfactory postoperative results are attributable to one or more of the following causes: (1) failure to restore the kidney to its proper position, (2) production of excessive trauma about the renal pedicle or the ureter at the time of operation and (3) failure to recognize coexistent pathologic changes in the kidney or adjacent organs.

Calculi.—Marion⁷ stated that after the successful removal of renal, pyelic or ureteral stones the general condition of the upper portion of the urinary tract in some cases is disappointing, as the patient frequently continues to suffer from urinary disturbances. In some cases an existent infection continues, or the kidney performs its excretory duties poorly; pockets may exist which have become cicatrized, and in the course of a few years pyonephrosis supervenes. Another tendency of kidneys that have been calculous is toward sclerosis. The kidney atrophies and becomes deformed; and the calices and pelves take on atypical characters, notwithstanding the fact that no fresh calculi have formed.

In some cases in which a ureteral calculus has been removed in the expectation that the patient would be relieved of urinary troubles, relief has failed to materialize, and, instead, the ureter has become cicatrized and its canal totally obliterated. This obliteration progresses silently and results in considerable atrophy of the kidney on the same side. Several cases were cited to illustrate these various pathologic changes. In some cases in which it might have been possible to reconstruct a working ureter, the function of the kidney continued to be deficient. In

7. Marion, G.: De l'évolution des reins après l'ablation des calculs du rein, du bassin et de l'uretère, *J. d'urolog.* **42**:193-204 (Sept.) 1936.

other cases so much periureteritis was present that the continuity of the ureter could not be restored, and the patient must carry a urinary fistula all his life because of changes in the ureter and the kidney.

From all these cases Marion concluded that the prognosis in operations for suppression of reno-ureteral calculi must be reserved, since without reappearance of calculi lesions may be established as the result of sclerosis, which finally lead to destruction of an organ which it had been hoped could be saved by removing the cause of the primary infection.

[COMPILERS' NOTE.—It should be borne in mind that the removal of calculi from the upper portion of the urinary tract is only the beginning of the necessary treatment. It is essential after removal of the stones to institute measures to secure good drainage and to relieve the infection. These two desiderata can be readily obtained by nephrostomy followed by routine cystoscopic treatments with dilations of the ureters and lavage of the renal pelvis. These treatments should be carried out at first once a week, then once in two or three weeks and later once a month; it may even be necessary to repeat them once or twice a year for a long period. Finally, the urologic condition of the patient should be checked occasionally for a reasonable length of time by intravenous urograms, and sometimes a special dietary regimen also should be instituted.

When such control is not properly maintained, we must agree with Marion that the outcome of surgical intervention for relief of nephro-ureterolithiasis is very poor, particularly in clinic cases in which the condition is beyond control. But when the fundamental principles of drainage, relief of infection and administration of a proper diet are carried out under the systematic control of a follow-up clinic, the results are gratifying.]

Priestley and Osterberg⁸ briefly discussed the current theories of the etiologic factor of renal calculi, namely, stasis, infection, vitamin deficiency, other dietetic errors, metabolic disorders, endocrine disturbances, abnormalities of the p_H of the urine, various alterations of the urinary colloid-crystalloid relationship, local ulcerating lesions in the collecting portion of the kidney, etc. It seems unlikely that the etiologic factor is the same in all types of calculi. For example, cystine, urate and phosphate stones are obviously formed by a different process.

The authors studied 193 cases in which stones composed chiefly of calcium oxalate, of calcium phosphate associated with varying amounts of calcium carbonate or of urates were removed from the urinary tract. In each case the chemical composition of the stone was determined.

8. Priestley, J. T., and Osterberg, A. E.: The Relationship Between the Chemical Composition of Renal Calculi and Associated Bacteria, *J. Urol.* **36**:447-459 (Oct.) 1936.

and in many cases the preoperative p_H of the urine was determined and cultures of the urine and calculi were made. Cystine, xanthine and other uncommon types of stones were not included in the study because the data on these calculi seemed insufficient to be significant. There were 93 oxalate stones, 71 phosphate stones and 29 urate stones.

It was noted that calculi of different chemical composition are not found with equal frequency in all parts of the urinary tract. For example, 82.8 per cent of the oxalate stones were removed from the kidney or ureter, and, in contrast, only 48.3 per cent of urate stones were removed from the upper part of the urinary tract. Approximately 62 per cent of the phosphate calculi were removed from the kidney or ureter, and the remainder were removed from the bladder. Apparently urate and phosphate stones form somewhat more frequently in the bladder than do oxalate calculi. It seems possible that the site of origin of a calculus may be of etiologic significance. It was found that approximately 25 per cent of the phosphate and urate stones were bilateral, whereas only 13 per cent of the oxalate stones were bilateral. The average incidence of bilateral calculi in cases of nephrolithiasis is approximately 15 per cent. Recurrent stones are more often composed of phosphates than of oxalates. The rapidly reforming stone is almost invariably of phosphatic origin, although the original calculus may have been of a different nature. In this regard it is mentioned that phosphates normally occur in the urine in much larger amounts than do urates or oxalates.

All types of renal calculi may be associated with infection; however, in some cases infection is apparently present prior to precipitation of the stones, and in other instances it is a secondary development. Phosphate stones were found associated with bacteria in the urine in approximately 59 per cent of cases, whereas oxalate stones were found in infected urine in only 28 per cent and urate stones in 21 per cent of cases. Cultures of the stones themselves usually correspond closely to the cultures of the urine, although this is not always true. Many different types of bacteria are found associated with calculi, *Escherichia coli* being found most frequently. The relatively high incidence of *Proteus ammoniae* in association with phosphate stones is emphasized. Multiple types of bacteria were found more often in the presence of phosphate stones than they were with any other type of calculus. The wide variety of organisms that may be present indicates that under proper circumstances many different types of bacteria may be associated with the precipitation of stone.

The importance of p_H of the urine in the etiology of lithiasis was considered. Although the exact chemical sequelae of variations in p_H are not clearly understood, the resultant changes in solubility, colloidal

protection against precipitation of crystalline material, ionic equilibrium and other factors may have an important influence on the formation of stones. The p_H of the urine was invariably higher when infection was present. Normally, phosphate stones are associated with the highest p_H , oxalate stones with a somewhat lower p_H and urate stones with the lowest p_H of all.

Barney and Mintz⁹ stated that although hyperparathyroidism is responsible for between 4 and 5 per cent of all cases of urinary stone, in almost 70 per cent of the cases of this disease stones may be present. It is also true that in about 38 per cent of cases of hyperparathyroidism patients may have pathologic changes in both the bones and the urinary tract. This disease does not seem to be a factor in the production of bilateral urinary lithiasis. The symptoms and signs of urinary lithiasis in cases of tumor of the parathyroid glands do not differ from those attributable to other causes. After removal of the tumor stones do not recur. Barney and Mintz expressed the belief that today no physical examination is complete without a careful study of the calcium and phosphorus content of the blood, especially if urinary lithiasis is present or is suspected.

Higgins¹⁰ stated that diet is of definite benefit to the following groups of patients and that the best results are secured among such patients:

In the first group are the patients in whom there is a tendency to the recurrent formation of calculi after operation. A review of the cases at the Cleveland Clinic up to 1932 revealed recurrence in 16.4 per cent, but since a special diet has been prescribed as a routine after operation, this has been reduced to 4.7 per cent. Higgins stated that it may be too early to report these figures, for two years is the maximal period since operation, but he definitely expressed the opinion that a dietary regimen should be included in the postoperative care in addition to the therapeutic procedures employed previously. By following this principle, the cause and not the effect alone of the disease is treated.

In the second group of patients are those who have passed stones at frequent intervals but in whom larger calculi cannot be demonstrated in the kidney. At the Cleveland Clinic 40 of the patients in this group have been free from symptoms for two years.

The third group consists of orthopedic patients in whom stones develop while they are in the hospital. As a general rule, the stones are

9. Barney, J. D., and Mintz, E. R.: The Relation of the Parathyroid Glands to Urinary Lithiasis, *J. Urol.* **36**:159-167 (Aug.) 1936.

10. Higgins, C. C.: Urinary Lithiasis: Experimental Production and Solution with Clinical Application and End-Results, *J. Urol.* **36**:168-177 (Aug.) 1936.

composed of calcium and magnesium phosphate, namely, stones which form in an alkaline urine. If the high vitamin A acid ash diet is prescribed for these patients while they are forced to remain in a recumbent position, thus shifting the reaction of the urine to the acid side, the chemical possibility of the development of such calculi is reduced to a minimum.

Higgins seemed to be quite certain that if the patients who live in those communities in the United States which have been reported as stone areas could receive adequate amounts of vitamin A, the formation of calculi could be prevented in a large percentage.

It is difficult to say when stones will undergo dissolution. In one case a stone had not changed in size for eleven months until an attack of colic occurred recently. The stone was situated in the lower calix of the kidney, and some days after the attack of colic a considerable amount of sand was passed, and the large stone disappeared. On the other hand, in many cases response is not secured; the reason for this is not known. In an effort to explain this, Higgins is studying the outer coating of the stones and making a more careful quantitative analysis of them. After operation the renal pelvis is lavaged with 1 per cent solution of phosphoric acid, as suggested by Randall.

Higgins has studied a series of more than 35 cases in which complete urologic examination revealed renal calculi. These stones have been caused to undergo complete dissolution and have disappeared after the patient had followed the prescribed dietetic regimen.

In view of the fact that patients who have a duodenal ulcer and who are treated by the Sippy routine are given considerable amounts of alkali and as a general rule have a strongly alkaline reaction of the urine, Higgins expressed the belief that cod liver oil or halibut liver oil should be prescribed as a routine. He emphasized this because many cases have been reported in which calculi developed or were passed while the patients were being treated by this method.

Higgins,¹¹ in discussing prevention of recurrent renal calculi, stated that recurrent calculus formation occurs with sufficient frequency to be a seriously complicating factor in the surgical treatment of nephrolithiasis. Empirical treatment which has been employed in the past does not reduce the percentage of recurrence below 10 or 15. The alkaline or acid ash diet with a high vitamin A content should be prescribed after operation, the constituents of which depend on the p_H of the urine and the chemical constituents of the calculus. A group of 31 patients who previously had had frequent attacks of renal colic and had expelled

11. Higgins, C. C.: Prevention of Recurrent Renal Calculi, *Surg., Gynec. & Obst.* 63:23-34 (July) 1936.

small stones spontaneously have been free from symptoms for more than two years on dietary management. During the past four years, since this diet has been used in conjunction with other therapeutic agents, renal calculi have recurred in 4.7 per cent of the cases studied. This percentage, which is higher than was anticipated, was believed to be attributable to the fact that roentgen examination was not performed as a routine after operation and, thus, that some of the recurrences may have been false in type.

Hydronephrosis.—Campbell¹² reported a case of hydronephrotic renal destruction secondary to a ball-valve papilloma at the pelvic outlet. Chief interest focuses on the diagnosis; attention is directed to the urographic filling defect caused by the growth but which might justifiably be thought to be produced by a nonradiopaque calculus. Nephrectomy is the usual treatment.

Ormond¹³ reported 6 unsuccessful operations for hydronephrosis, 5 of which were for obstruction at the ureteropelvic juncture. Of the latter, 2 were converted into apparent successes by second operations. Experiences such as these do not warrant dogmatic or authoritative statements. Ormond stated that in view of this experience and in view of the results reported in the literature he was justified in drawing the following tentative conclusions:

The Heineke-Mikulicz type of operation should be distrusted in the future. It seems to be best suited to cases in the early stage in which there is no infection, and in many such cases reimplantation of the ureter has given satisfactory results. Ureteropyeloplasty has no advantages over reimplantation. It is rather difficult to perform with precision, for the kidney and the ureter are drawn up out of their natural positions in order to obtain exposure, and the line of incision and repair might be distorted when the organs are restored to their normal positions.

Resection of the ureteropelvic juncture should be favored, and the ureter should be cut on a slight bias to lessen the likelihood of stricture from contraction of the suture line and reimplanted into the lowest portion of the pelvis, with accurate apposition of the cut edges. The ureter should not be allowed to protrude into the pelvis at all. This is not difficult, and with a catheter running through the cortex and pelvis of the kidney and down the ureter, the first sutures nearly always can be made as the ureter and pelvis lie in situ. In every case a splinting catheter should be used, there being no haste about removal. In the

12. Campbell, M. F.: Hydronephrosis Due to Ball-Valve Obstruction by Papilloma at Ureteropelvic Junction, *Am. J. Surg.* **33**:291-293 (Aug.) 1936.

13. Ormond, J. K.: Unsuccessful Plastic Operations for Hydronephrosis, *J. Urol.* **36**:512-528 (Nov.) 1936.

presence of acute, or marked, infection, preliminary nephrostomy should be performed. In every case in which the kidney is not bound down by adhesions, preventing mobility, nephropexy should be performed.

Plastic operation should be reserved for those cases in which conservation of renal function is imperative or for those cases in which the desirability of conservation of renal function outweighs the chance of increased expense, danger and loss of time.

Campbell¹⁴ stated that vascular compression of the ureter is not uncommon in children. Vessels which produce the obstruction are congenitally anomalous. Hydronephrosis is the important uropathy, and infection usually is present. The commonest symptoms are pain in the renal region, pyuria, hematuria, a mass in the loin and, after the advent of infection, fever. Most children with vascular obstruction of the ureter are treated for months for chronic pyelitis. In the absence of infection, the renal changes, as interpreted by urinalysis, are regularly diagnosed as those of chronic interstitial nephritis. Yet the correct diagnosis usually can be made preoperatively by a complete urologic examination. The correct diagnosis is often suggested by the excretory urogram. Delayed diagnosis and radical surgical treatment are usually reciprocal. Nonoperative treatment has no place. Conservative surgical treatment may be expected to save a gratifying number of injured kidneys. Unfortunately the medical profession is as yet insufficiently alert to the high incidence and importance of urologic disease in children. Because of the consequent delay in making the diagnosis, nephrectomy will necessarily be the treatment for fully half of the children with vascular ureteral blockage.

Renal Abscess.—Emmett and Priestley¹⁵ reported a case of solitary renal abscess. The original roentgenogram of the urinary tract revealed a large shadow of a soft tissue mass in the left side of the abdomen. The shadow of the psoas muscle on the left side was much less distinct than that on the right. An intravenous urogram revealed a normal right kidney. The pelvis of the left kidney, which was approximately normal in size, was flattened on its lateral aspect by a soft tissue mass situated in the region of the lower pole of the kidney. The calices were elongated and distorted. The upper calix was flaring at its tip, and the middle calix was flattened against the pelvis. The lower calix was only partially visualized, and obliteration of its lower part was suggested.

At operation the upper half of the kidney appeared to be normal, but in the lower pole there was a large inflammatory mass which was

14. Campbell, M. F.: Vascular Obstruction of the Ureter in Children, *J. Urol.* **36**:366-387 (Oct.) 1936.

15. Emmett, J. L., and Priestley, J. T.: Solitary Renal Abscess (Carbuncle): Report of Case, *Proc. Staff Meet., Mayo Clin.* **11**:764-767 (Nov. 25) 1936.

densely adherent to the peritoneum and adjacent structures. During mobilization of the lower pole, some nonodorous pus was encountered. Nephrectomy was performed. The tissues, including the peritoneum, which had surrounded the lower pole, were indurated, inflamed and thickened. This region was packed with iodoform gauze, and the wound was closed loosely with a few interrupted sutures. In the lower pole of the kidney there was a large, well circumscribed abscess, with multiple points of discharge typical of the so-called renal carbuncle.

In contrast to the majority of renal lesions, the correct preoperative diagnosis of renal carbuncle is usually difficult to make, primarily because no characteristic deformity is revealed in the urogram. If the lesion is small, the outline of the pelvis and calices may be perfectly normal; if it is large enough to produce deformity, this deformity frequently simulates that of a neoplasm or cyst. In the roentgenogram diminution in intensity or absence of the shadow of the psoas muscle on the affected side, associated with scoliosis of the spinal column, may call attention to the condition, especially if considerable perinephritis is present.

Carbuncle of the kidney, like a smaller unilocular cortical abscess, is considered a manifestation of a blood-borne infection. It usually develops slowly over a period of some weeks or months, during which interval there is a paucity of symptoms. Depending on the duration and extent of the process, perirenal involvement will be slight or extensive. Treatment is surgical and consists of either resection of the carbuncle or nephrectomy. Removal of the kidney is usually advisable if the other kidney is normal, as conservative procedures are often followed by prolonged convalescence and nephrectomy may be necessary in the end.

Tuberculosis.—Mazzarelli¹⁶ carried out experiments consisting of the inoculation of tubercle bacilli into the perihilar tissue of the kidney and into the wall of the ureter, by which he was able to produce tuberculosis of the renal pelvis and the corresponding renal parenchyma.

In the majority of the experiments inoculation was followed by generalized tuberculosis, which included also a renal localization. The tubercle bacilli evidently came to the kidney by way of the blood stream. In some cases, however, the tuberculous changes were strictly confined to the zone of inoculation, that is, to the corresponding kidney and the regional lymph glands, without any localization in other organs; in these instances diffusion to the kidney by way of the blood stream must be excluded, and diffusion by the lymphatics must be assumed. These cases were relatively rare, but they prove that this mode of infec-

16. Mazzarelli, M.: Considerazioni e ricerche sulla patogenesi della tubercolosi renale, Arch. ital. di urol. 13:119-166 (March) 1936.

tion of the kidney is a possibility. Infection by this route has been admitted in cases of pulmonary localization, and there is no reason why it should not be possible for other organs as well. All authors agree that tuberculosis of the kidney is practically always secondary, although Albarran collected from the literature reports of 6 cases of primary renal tuberculosis. After an extensive review of the literature, Mazzarelli pointed out that ascending infection was once believed to be the common route for renal tuberculosis, Albarran himself being among those who held this view. Today, however, it is believed that this is the route only under favorable conditions, such as exist when the sphincter of the ureteral meatus is weak or absent, so that vesicorenal reflux occurs.

The deep and superficial lymphatics of the kidney and also those of the fatty capsule empty into the corresponding para-aortic lymph nodes, which thus become the regional lymph nodes of the kidney. But these may also receive lymph from other abdominal and pelvic organs, such as the hilus of the kidney, the ureter, bladder, urethra, prostate gland, seminal vesicles and testes; all of these lymphatics were traced by the author. Between all of these lymph channels there are anastomoses, and any of them may flow into the same abdomino-aortic ganglions. In the lymphatic infection of the kidney three routes were distinguished: (1) the ascending ureteral route, (2) the retrograde route and (3) the route from nearby organs. Experiments were done to discover whether renal tuberculosis could be produced by the lymphatic route, through infection of the ureteral walls or the tissues about the pelvis or hilus, whether an inflammation of the testis could be started by the lymphatic route and, finally, the modes by which this infection is developed. The author found that he could produce specific changes which often remained localized at the point of inoculation or in nearby zones but were sometimes diffused. Thus, after one hundred and eighty days he found tuberculosis localized exclusively to the kidney or ureter in 4 of 25 experiments, which gives a relatively high percentage. In the other experiments there was most often a generalized tuberculosis, with concomitant renal lesions, which had developed because of injection by the hematogenous route, and therefore these were not counted. Apparently the bacilli are diffused along the submucous spaces, where there is a rich lymphatic network, and in cases of lymphatic infection they are carried upward by the lymphatic current to the renal pelvis.

Sutherland and Braasch¹⁷ reviewed the development of the roentgen ray and its use in urologic diagnosis. Important anatomic character-

17. Sutherland, C. G., and Braasch, W. F.: The Value of Roentgen Rays in the Diagnosis of Renal Tuberculosis, *Tubercle* **17**:309-317 (April) 1936.

istics of the kidney were emphasized in their relation to the roentgenographic diagnosis of tuberculosis. The pathologic changes caused by early tuberculosis in the kidney were considered. A review was made of 1,314 cases in which the patients were treated surgically and the presence of renal tuberculosis was proved by microscopic examination. In 1,157 of these cases a preliminary plain roentgenogram of the genito-urinary tract was made, and in 237 cases (20.6 per cent) the findings were positive; that is, some abnormality was present which suggested the presence of a lesion in the genito-urinary tract. These abnormal findings included alteration in the size and contour of the soft tissue shadow of the kidney; more or less extensive calcification in the region of the kidney, which was occasionally misinterpreted as evidence of renal calculi; indeterminate types of shadow, and calcified lymph nodes. In the roentgenogram the margin of a tuberculous calcified area is usually rough and irregular, whereas that of a calculus tends to be more discrete and smooth in outline. Shadows of tuberculous calcifications are found more frequently in the region of the cortex, whereas those of calculi are commonly seen in the pelvis or in the calices. There is frequently a difference in the intensity of the shadow cast by a tuberculous lesion in contrast to that cast by a renal calculus. As mentioned previously, there was some evidence of abnormality in the plain roentgenogram in approximately a fifth of all cases. Retrograde and excretory urography were then employed in order to establish a definite diagnosis. At times excretory urography alone gives sufficient information on which to base diagnosis and treatment. Frequently, however, cystoscopy and retrograde pyelography are essential.

It is the consensus that renal tuberculosis is never a primary condition. In this series roentgenographic examination of the thorax was made in 911 cases. In 280 cases (30.7 per cent) there was evidence of pulmonary tuberculosis, which in the majority of cases was latent. In 83 of 1,314 cases tuberculous lesions were coexistent in bone. Fortunately, at present patients consult the physician earlier than they did formerly. Today renal tuberculosis is suspected when dysuria persists over a period of one or two months; the urine is stained for tubercle bacilli, and in cases in which the diagnosis is doubtful guinea-pigs are inoculated, cystoscopic examinations are made, the kidneys are catheterized and pyelograms are made. Renal tuberculosis in the advanced stage with severe ulceration and deformity of the bladder is encountered less commonly. It is generally believed that the condition is hematogenous and begins in the kidney rather than in the bladder. The infecting agent passes through the capillary system of the glomeruli and settles in some portion of the collecting system. Then, by a retrograde process, it

passes up the lymphatic structures and infects the cortex. The lesion is probably unilateral in the beginning and may remain so for a remarkably long time. The incidence of primary bilateral renal tuberculosis, on the other hand, is probably greater than was previously supposed; the possibility of spontaneous recovery in the early miliary type of renal tuberculosis must be recognized. The importance of pre-operative and postoperative hygienic treatment in assuring the best prognosis cannot be overemphasized.

Definite limitations and possibilities of error in the use of the excretory urogram as a single method of diagnosis in cases of renal tuberculosis are mentioned. In the differential diagnosis the changes resulting from pyogenic pyelonephritis are most frequently confused with those of tuberculosis. In the urogram deformity occurring with pyelonephritis tends to be more commonly uniform; all of the calices are likely to be involved by inflammatory dilatation, and evidence of cortical involvement is much less frequent. In the retrograde urogram artefacts from overdistention or incomplete distention may simulate tuberculosis, and extravasation may cause shadows in the parenchyma distal to the tips of the minor calices which may be confused with those of cortical necrosis as a result of tuberculosis. Likewise, nephrolithiasis, when associated with pyelonephritis or pyonephrosis and cortical abscesses, may simulate tuberculosis closely in its urographic manifestations. Tuberculosis may invade the perinephric tissues, and the outstanding roentgenographic evidence will be obliteration of the shadow of the psoas muscle on the affected side. Carcinoma of the kidney not infrequently is attended by calcification in the primary tumor, and such calcification may be mistaken for tuberculosis. Likewise, necrosis may be caused by malignant involvement. Roentgenography does not play an important part in the identification of tuberculosis in the genital organs.

Weber¹⁸ found that in nearly all instances the end of the ureter which had been sewed into the skin after nephrectomy for tuberculosis contained tubercle bacilli on culture on the second and third postoperative days. He considered this as a proof that the stump of the ureter is often the source of a fistula. In his cases the formation of a fistula postoperatively was much rarer when the ureter was cut after the renal pedicle was clamped and then tied and brought out to the skin. He recommended this as a standard procedure in nephrectomy for tuberculosis.

18. Weber, Herbert: Zur Vermeidung postoperativer Fisteln bei Nierentuberkulose (Tuberkelbacillenkulturen aus dem Ureterstumpf), *Ztschr. f. urol. Chir. u. Gynäk.* 42:416-428 (Dec.) 1936.

Pelz¹⁹ stated that the microscopic examination of a stained smear of the urinary sediment in cases of renal tuberculosis often gave negative results. Results of inoculation of guinea-pigs are usually positive, but the method necessitates waiting too long. The culture method of Löwenstein gave positive results in 88 per cent of cases of renal tuberculosis and in 55 per cent of the cases of tuberculous epididymitis. Fifty-five patients were examined. It is interesting to note that sometimes cultures of blood were positive for tuberculosis at an earlier time than the cultures of the urine.

Hemorrhagic Cysts.—Barney²⁰ reported 2 cases of hemorrhagic cyst of the kidney. The hemorrhage in case 1 was acute and gave rise to a train of obscure subjective and objective symptoms. The etiology was unknown, but the possibility of infection or trauma and perhaps embolism or thrombosis should be considered. The presence of another cyst in the same kidney, which was thin walled and filled with serous fluid, increased the probability that what ended as a hemorrhagic cyst might well have started as a serous cyst.

In case 2 nothing was known of the antecedents of the condition. The fact that the kidney opposite to the one which contained the hemorrhagic cyst contained three serous cysts might allow one to follow the same train of thought as in case 1. On the other hand, the calcified wall surrounding the blood clot would indicate an ancient process, with symptoms so insignificant that the patient did not notice them.

In case 1 there were no symptoms, subjective or objective, previous to the onset of the hemorrhage. At this time the symptoms were very suggestive of renal colic, caused perhaps by calculus. There was in addition a strong suggestion of a rather severe but obscure hemorrhage. The pain and tenderness can be accounted for by the sudden increase of tension within the cavity of the cyst.

In case 2 there were evidently no signs or symptoms during life which could be elicited by the history or physical examination. The calcified wall of the cyst is indicative of a long-standing process, and the hemorrhage into it was not extensive enough to have caused symptoms at the time it occurred.

These 2 cases illustrate that cysts of the kidney may, and in fact often do, exist for an indefinite and probably a long time without giving rise to symptoms. The factors which bring about their recognition are pressure, pain, the presence of a tumor, intracystic pressure and acute hemorrhage.

19. Pelz, S.: Nachweis der Tuberkelbazillen bei Urogenitalerkrankungen durch das Kulturverfahren nach Professor Löwenstein, Wien. med. Wchnschr. 86:1027-1029 (Sept. 5) 1936.

20. Barney, J. D.: Hemorrhagic Cyst of the Kidney. J. Urol. 36:602-608 (Dec.) 1936.

Hydatid Disease.—Begg²¹ stated that a total of approximately 800 cases of hydatid disease of the kidney is available for study. The incidence of the disease fluctuates in a given country with the number of sheep, the living conditions, the level of culture and the efficacy of preventive measures.

Renal cysts may be classed according to their relation to the renal pelvis as open, closed and pseudoclosed. In the first type both the pericystic and the endocystic cavity communicate with the pelvis; in the second type neither cavity communicates with the pelvis, and in the third type, only the pericystic cavity, the ectocyst remaining unruptured. Symptoms are characteristic for each type of cyst. In the open cyst they consist of renal colic and the passage of hydatid elements in the urine; in the closed cyst the symptoms are usually attributable to pressure; in the pseudoclosed cyst the typical manifestations are intermittent attacks of pain localized to the loin due to colicky pain of the calix and perhaps urinary symptoms, such as hematuria or frequency, but no hydatid material is passed.

The etiology of hydatid disease of the kidney is that of hydatid disease in general. The industry of sheep raising, on the one hand, and insanitary conditions of life, on the other, contribute chiefly to its incidence and spread.

Unlike the liver, the kidney is almost invariably the site of one primary cyst only. In the larger series of cases the incidence of involvement of each kidney is equal, and bilateral cysts are rare. Nicaise found involvement of the right kidney in 197 cases, of the left kidney in 185 cases and of both kidneys in 12 cases. The sexes are equally vulnerable. Most patients are infected in childhood, and the third to the fifth decade is the commonest period for the development of symptoms. In the reported cases the youngest patient operated on was a child aged 2 years. The commonest site of the cyst is the cortex of the anterior surface at the upper and lower poles.

In the kidney, as elsewhere, the hydatid cyst develops slowly, though growth may be stimulated by trauma or pregnancy. Expansion is centrifugal, but the center point of the sphere is not static. As a rule the line of least resistance is followed, but in an effort to preserve its circular contour the cyst may burrow into the spleen, into the liver or into the tail of the pancreas. The hydatid may die of old age or lack of nutriment. There is a ring of large blood vessels in the pericyst, a striking feature microscopically. Thus ample serum is brought to the hyaline laminated membrane, from which the parasite can select its food supplies. Calcification hinders the osmotic process. The animal

21. Begg, R. C.: Hydatid Disease of the Kidney, *Brit. J. Surg.* **24**:18-40 (July) 1936.

feels the urge for more defensive propagation. Daughter cysts are born in large numbers and even granddaughter cysts. Tension may become low, and growth may be in abeyance or spasmodic. The whole tribe may perish and be buried in lime, or sepsis may supervene. Low grade life may, however, be maintained, even though the pericyst is heavily calcified.

The expanding pericyst may become incorporated in the stomach, spleen, pancreas, colon, liver, duodenum or vena cava. The adrenal glands may become inseparably fused. Such a welding of tissues becomes a danger at operation, chiefly if the surgeon confuses it with an ordinary adhesion and attempts to separate the inseparable. There is no reason why a large cyst at the upper pole should not rupture into the bronchial system. Complications within the urinary tract include hydronephrosis, pyonephrosis, lowering of capacity of the kidney on both sides from difficulty in micturition or chronic retention from an accumulation of membrane in the bladder, with or without bilateral ascending pyelonephritis. All are rare and usually are attributable to sepsis. The ureter on the affected side may become completely occluded.

Calculus associated with hydatid cyst is rare, even in such countries as Dalmatia, in which both conditions are common.

Symptoms may not appear for many years, and the patient may be ignorant of the existence of the cyst till the day of his death. A closed cyst may be found accidentally in a person who is perfectly well. The parasite may produce unexplained anaphylactic phenomena, such as urticaria or symptoms of obscure pressure. A closed cyst that grows toward the abdomen causes indigestion, pain and fulness after meals by encroaching on the stomach, or diarrhea, constipation or even complete obstruction by pressure on the colon.

In the case of an open cyst diagnosis is made from examination of the material passed. If this is only hydatid sand or brood capsules, the condition may be considered as merely caused by the passage of gravel, and the patient may have to wait some time before a microscopic examination of the sediment discloses hooklets and scolices. A calcified cyst may produce solid débris, which when passed is mistaken for calculus. A pseudoclosed cyst is demonstrated by a typical pyelogram. A closed cyst is most difficult to demonstrate. Clinically, it appears as a tumor of the hypochondrium or as a free and mobile tumor of the abdominal cavity. If the muscles are rigid, such a tumor may be missed during an attack of renal colic. The commonest error in diagnosing a tumor in the hypochondrium is to mistake a cyst on the left side for an enlarged spleen, especially in communities in which malaria is endemic, or one on the right side for a cyst of the liver. In the case of the former the special serum tests, with roentgen examina-

tion and pyelograms, usually clear up the diagnosis; in the case of the latter, serum tests are useless. A cyst at the upper pole of the kidney may produce a high area of dulness at the base of the lung of the corresponding side and has to be distinguished from an intrathoracic condition or a splenic cyst as well as from hydronephrosis. The greatest calamity in such cases is a diagnostic puncture. When there are no physical signs, routine urologic examination may reveal deformity of the renal pelvis, and the serum tests may eliminate other confusing renal conditions.

Roentgenographic examination may reveal a density due to the high saline content of hydatid fluid or a typical curvilinear shadow of a calcified pericyst. In all types of cases complete urologic investigation usually gives fairly conclusive information.

The precipitin test is rarely used. The complement fixation test, worked out by several persons, is a laboratory procedure requiring rigid conditions of technic to give its best results. The intradermal reaction of Casoni, taking into account both the immediate and the delayed reaction, is simple, practical and of great value.

From the statistics available, hydatid disease of the kidney appears on the whole to be relatively innocuous. Of the 474 cases of Nicaise, 20 per cent were found in the course of routine postmortem examination; 215 of the patients received no surgical treatment, and only 16 died as the direct or indirect result of the cyst. The first attack of colic and the passage of membrane may be the last in spite of an active parasite. Impairment of renal function to a dangerous level is rare even in cases of long standing, and the general health of the patient is seldom affected. Spontaneous cure occurs in many cases, though symptomatic cure is probably more common than anatomic.

Treatment is mainly surgical or expectant. Turpentine has been used to assist elimination of the daughter cysts. No intravenous therapy is effective. Nephrectomy was introduced by Bockel in 1887 to replace the universal method of marsupialization. Intervention must be governed by two considerations: In the first place the disease is benign, and a cyst once communicating with the pelvis as a rule ceases to grow because the level of tension required in the fluid for this purpose reopens the safety-valve. In the second place radical operation is difficult because of the dense adhesions and is not to be undertaken lightly.

As a rule operation is not indicated in the following circumstances: 1. After a first attack in which cysts are passed in the urine when investigation reveals that only a small cyst is present and that renal function is good on both sides. The danger of complications is small, and subsequent intervention may be undertaken if disabling symptoms or septic complications occur. 2. If the other kidney is absent, infantile

or functioning badly from any cause and no serious disability is caused by the hydatid. In the best hands any difficult operation on a kidney may lead to damage demanding nephrectomy, and the risk of operation is greater than that of the parasite. 3. If the cyst is calcified and dead, unless passage of the calcified fragments threatens damage to the urinary tract or is seriously disabling.

In most other cases nephrectomy, if possible, is the operation of choice if the other kidney is normal in function, for the following reasons: 1. The mortality is low, convalescence is short and health is quickly restored. 2. Secondary cysts may exist in the calix, making recurrence inevitable if the kidney is left. These cannot be detected during any conservative operation. 3. An apparently closed cyst may really be of the pseudoclosed type, and with conservative operations there is danger not only of recurrence but of infecting the urinary tract. 4. In many cases the whole of the pericyst cannot be removed, and in these instances recurrence is common. If the kidney is left, the old symptoms of renal colic and the passage of membrane will recur. When the kidney is removed, the recurring cyst will cause no trouble and in the course of many years will reach the surface in the loin, where it can be easily dealt with.

Circulation.—Anson, Richardson and Minear²² studied the variations in the number and arrangement of the renal vessels of 400 kidneys. In only 35 per cent of 200 consecutively examined cadavers were the renal arteries of both sides arranged in the simplest pattern, namely, with a single vessel supplying each kidney. In 65 per cent of the 200 cadavers a unilateral or a bilateral anomaly of the renal arteries was present, a condition so regularly prevailing that it certainly should no longer be regarded as anomalous. In 20 per cent of the bodies the simple arrangement of renal vessels occurred on the right side, accompanied by supernumerary arteries on the left side; in 17 per cent, a single vessel supplied the left kidney and multiple vessels the right; in 28 per cent, multiple vessels supplied the right kidney, and in 28 per cent, multiple vessels supplied both kidneys. Of the 400 kidneys, 53 per cent were found to have a so-called normal arterial supply. The remaining 47 per cent possessed extra-arterial branches.

The authors encountered no kidney in which the number of supernumerary vessels exceeded four (three from the aorta to the hilus and one from the renal artery to the extremity). From the data obtained

22. Anson, B. J.; Richardson, G. A., and Minear, W. L.: Variations in the Number and Arrangement of the Renal Vessels: A Study of the Blood Supply of Four Hundred Kidneys, *J. Urol.* **36**:211-219 (Sept.) 1936.

on the renal tributaries of the inferior vena cava in the same group of 400 kidneys, it is strikingly evident that venous variations are relatively few.

Hyman²³ made a study of 6 cases of suppurative disease of the kidney complicated in 5 instances by suppurative thrombophlebitis of the renal vein; the diagnosis was confirmed by operation or postmortem examination. Since this condition is nearly always secondary to a suppurative lesion in the kidney, the diagnostic criteria are not sufficiently clearcut to differentiate thrombophlebitis from the primary disease of the kidney, which in 5 cases was a cortical abscess. The clinical picture is essentially one of sepsis with or without bacteremia. If sepsis is not controlled after adequate drainage of a suppurative focus in the kidney or after nephrectomy, thrombophlebitis of the renal vein should be suspected. It should be realized that the kidneys are often the seat of localized metastatic abscesses following cutaneous staphylococcic infections. With this type of infection, invasion of the blood stream by staphylococci not infrequently occurs. If after drainage operation and decapsulation of the kidney, the sepsis persists, nephrectomy should be done and the renal vein ligated as close to the vena cava as possible. If the sepsis persists after a primary nephrectomy, the renal vein should be suspected and explored.

Operation disclosed in 2 instances that thrombophlebitis may be present without causing any recognizable gross changes in the vein. This study further disclosed that in 3 instances the thrombotic process at the time of nephrectomy had already extended into the vena cava. One can well realize that under such conditions nephrectomy even with wide ligation of the renal vein might prove futile.

These 5 cases indicate definitely that suppurative lesions of the kidney act as a source of invasion of the blood stream by the production of a secondary thrombophlebitis. The mortality from this condition is unusually high, because in most instances the sepsis is already widespread before the nature of the disease is recognized.

Pain Syndromes.—Keyser²⁴ has previously advanced the proposition that pain in the upper part of the urinary tract occurs not infrequently when a small, if any, lesion can be demonstrated clinically and that after repeated scrupulous examinations from many points of view other than urologic, one is at a loss to understand the fundamental pathologic process involved. He presented the hypothesis, and some evidence substantiating it from a series of 60 cases, that nodal spasm of neurogenic

23. Hyman, Abraham: Acute Suppurative Thrombophlebitis of the Renal Vein, *J. Urol.* **36**:196-210 (Sept.) 1936.

24. Keyser, L. D.: Pain Syndromes in the Upper Urinary Tract: Their Mechanisms and Clinical Management, *South. M. J.* **29**:953-963 (Oct.) 1936.

background can simulate ureteral stricture and that the clinical course of most of his patients warranted the belief that spasm rather than organic stricture was most often the pain-producing mechanism.

He stated: "The differentiation of organic ureteral stricture and of localized nodal spasm is of prime importance. However, this is frequently difficult and at times impossible." One may consider the following criteria: The reproduction of pain on the passage of a bulb bougie or the injection of fluid is presumptive evidence that the seat of the trouble has been found. Keyser stated that the production of pain in this manner does not differentiate spasm from stricture. The bulb bougie, even though it should hang consistently at the same site, does not differentiate spasm from stricture, as the hang may be due to either. With the patient under a good high spinal anesthesia, however, one expects spasm to abate and organic stricture still to be resistant. This is usually, but not always, the case.

Repeated urography with some form of serial plate taking is important. In most instances stricture will show persistent dilatation above its site, while spasm will be unaccompanied by such dilatation.

At present Keyser uses a three plate pyelographic method in the following manner:

. . . the first plate being taken in extreme Trendelenburg, the second and third as quickly as possible in reversed Trendelenburg or the upright position. In this way one obtains a serial bilateral retrograde urogram and acquires information as to the mobility of the kidneys as a whole, as well as to the variations of motor activity of the pelvis and ureter. . . .

After thorough ureteral dilatation with bulbs one would expect stricture to remain open longer than would spasm and to produce consequent relief of symptoms for a greater period of time. This, however, is not consistently true, as many spastic ureters are relieved indefinitely after the simple passing of the ureteral catheter. In the ultimate, absolute differentiation of stricture and spasm can be made only by operative or autopsy exposure of the obstructing site.

In considering the therapy of ureteral stricture and spastic reno-ureteral syndromes, Keyser stated:

The procedures to be considered are the dilatation of the ureter with bulb bearing bougies or catheters; the temporary splinting of the ureter with indwelling catheters; the surgical procedures, such as nephropexy, plastic operations on constricted areas, the resection of hydronephroses, and denervation operations on the renal pedicle or the ureter. . . .

In treating painful reno-ureteric syndromes, ureteral dilatation with bulbs and the use of the indwelling catheter have been the initial effort. I have in recent years used the indwelling catheter more and more, especially at the beginning. . . .

Dilatation is not practiced with acute or subacute infection. Here, if conservative measures of oral antiseptic therapy fail, the indwelling catheter is tried, and successively larger sizes are placed every four or five days. It is

remarkable how severe infection may clear up and what remarkable restoration of renal function ensues with a well draining ureteral catheter.

The indwelling catheter or dilation with bulb bougies has in Keyser's experience given complete to partial symptomatic relief in from 60 to 80 per cent of a large enough series of cases to warrant conclusions. He expressed the belief that conservative ureteral dilation is a method worthy of trial before operation is undertaken, not necessarily because of a high incidence of organic ureteral stricture, but as a therapeutic attempt to readjust an unbalanced neuromotor dysfunction.

Surgical Procedures.—Weiser²⁵ stated that if the pleura is opened during the course of an operation on the kidney it should be sutured immediately. He advised postoperative evacuation of the pneumothorax with one of the ordinary apparatus for pneumothorax suction by means of puncture and suction. Weiser had had occasion to carry out this procedure with complete success.

Sympathectomy.—Gibson²⁶ stated that renal sympathectomy produces no harmful effects on the kidney; it is surgically feasible either alone or in conjunction with other procedures, and in a number of conditions there are either relative or definite indications for its application.

Among the indications for renal sympathectomy is some type of renal sympatheticotonia, namely, spasm, atony, dyskinesia, hyperdynamic motility and adynamia, either alone or in association with definite organic changes, such as small hydronephrosis, nephroptosis, painful chronic nephritis, painful adhesive perinephritis, essential hematuria, certain types of Bright's disease associated with oliguria and anuria, unyielding reflex anuria and possibly certain stone-forming diatheses.

Renal sympathectomy is recommended, in conjunction with other necessary surgical procedures, as an extra precautionary measure to make doubly sure of complete relief in any case of proved renal pain in which careful investigation reveals few or no demonstrable pathologic changes to explain the symptoms adequately. Whether renal sympathectomy is undertaken as the primary object of a surgical attack on the kidney or is merely incidental to other procedures, no great technical difficulties are encountered if the precautions necessary for adequate exposure of the kidney are observed. The main bugbear of the operation is the possibility of injury to the renal vein, which is as thin walled as tissue paper. If one bears in mind that the nerve fibrils

25. Weiser, Arthur: Vorschlag zur Behandlung des bei Nierenoperationen durch Pleuraverletzung entstandenen Pneumothorax, *Wien. med. Wchnschr.* **86**: 1044-1045 (Sept. 5) 1936.

26. Gibson, T. E.: The Present Status of Renal Sympathectomy, *J. Urol.* **36**: 334-363 (Oct.) 1936.

are in the fascia immediately surrounding the renal artery and if the vein is avoided meticulously except to retract it away from the scene of action, this hazard is appreciably diminished. Experience has shown that the best strategy is to start mesially and work laterally toward the renal hilus. The fascia surrounding the vessels is pushed away with gauze sponges and smooth thumb forceps until the vessels are exposed, and the nerves which are then seen in bundles about the artery are picked up with a hook and resected with scissors. Gibson has found it easier in most cases to start the dissection anteriorly but to perform the major portion of it from the posterior aspect after retracting the ureter and the pelvis with a hernia tape. The artery is approached easily from the posterior aspect, whereas anteriorly it is covered by the vein. A hook is essential in picking up the nerves lying directly on the artery as well as for drawing out the fascia containing the nerves from between the artery and the vein. Great care must be taken that the point of the hook does not touch the vein. A small blood vessel retractor is useful at times in protecting the vein from injury. The dissection should not be carried too close to the renal parenchyma, because often small vessels are given off at this level which are easily broken, thus obscuring the field of operation with troublesome bleeding.

Oldham, after stripping the pedicle as clean as possible, swabbed it with a 10 per cent solution of phenol, which he stated did not injure the vessels or ureter and was strong enough to destroy nerve fibrils missed by the dissection. Phenol also reveals any nerve fibrils that may have been overlooked, and they can then be severed if it is so desired.

Secretion of Urine.—Snapper²⁷ stated that urine is formed only by the combined action of different physiologic processes in the kidney in which the functions of the glomeruli and tubules are separated completely. It has been proved beyond doubt that in the glomeruli an ultrafiltrate of the blood plasma is formed. The glomerular filtrate contains all crystalloid substances of the blood plasma in the same concentration in which they are present in the blood, but the colloids, especially the proteins, do not pass through the glomerular membrane. In the tubules a reabsorption of water and different substances takes place. During passage through the tubules the original glomerular filtrate is changed into definite urine. The study of the rate of excretion and concentration of certain substances, which pass into the glomerular filtrate, are not reabsorbed in the tubules and are not excreted in the tubules, has shown that an astounding quantity of

27. Snapper, I.: The Pathological Physiology of the Secretion of the Urine, Kong. d. internat. Gesellsch. f. Urol. 6:575-627 (Sept.) 1936.

glomerular filtrate is filtered off per minute. This quantity varies between 110 and 170 cc. per minute. From 97 to 99 per cent of the water of this glomerular filtrate must be reabsorbed in the tubules. Neither this rate of filtration in the glomeruli nor this excessive reabsorption in the tubules is impossible, as different experiments and calculations have demonstrated. The creatinine and inulin methods by which these data have been obtained have withstood criticism successfully. As a physical ultrafiltration of the blood plasma takes place in the glomeruli, blood pressure must be important for the function of the glomeruli.

The permeability of the glomerular membrane is to be compared with that of a collodion membrane. Substances with a high molecular weight are retained; substances with a low molecular weight pass. As a rule it may be stated that substances with a molecular weight of less than 40,000 appear in the glomerular filtrate, whereas colloids with a molecular weight of more than 60,000 are retained in the blood.

In case of renal insufficiency the composition of the urine and blood may be fundamentally changed. For a normal functioning of the kidneys, a normal composition of the blood plasma is necessary. Changes in the composition of the blood may be followed by serious disturbances of the function of the kidneys, so-called extrarenal uremia. A decrease of the protein content of the blood plasma and of the sodium and chloride content of the blood plasma may both have an adverse influence on renal function. The innervation of the kidney is of great importance in renal function. Reflex anuria may be explained in this way. It is still doubtful whether operations on the nerve supply of the kidneys improve the functions of the diseased kidney.

Urine is a supersaturated solution of many substances. Different substances, practically insoluble, are present in solution of the urine in large quantities. This problem is of great importance in the prevention of the formation of stones. The hydrotropic action of different organic constituents of the urine is considered. Urea and hippuric, salicylic and phenylglycolic (mandelic) acid, and other substances often present in the urine increase the solubility of calcium salts, especially of calcium oxalate. Besides this direct hydrotropic action, the stabilizing influence of these substances on the colloids of the urine is of importance in the prevention of the formation of stones.

URETER

Anomaly.—Malgras²⁸ said that the extravasical opening of a ureter in the female ordinarily produces a picture of incontinence that is so

28. Malgras, P.: Abouchements extravésicaux de l'uretère chez la femme. *J. d'urol.* 42:269-301 (Sept.) 1936.

characteristic that it will immediately suggest the correct diagnosis. It is a permanent incontinence, existing from birth, although micturition is normal. In cases in which the orifice of the ectopic ureter is discovered, retrograde pyelography will make it possible to determine to which kidney it belongs and also will reveal whether there is a double kidney, as is usually the case. Inability to discover such an orifice, however, should not be sufficient grounds for discarding the diagnosis of extravesical ureter if the clinical syndrome is clear. In that case an attempt should be made to demonstrate the abnormal kidney corresponding to this ureter. At present urography seems to be the most precise method for bringing out this evidence, provided more is not demanded of it than it can give. It makes it possible to affirm the existence of a supernumerary pelvis when such an organ is made visible by some opaque medium, but it does not justify the denial of such a pelvis when this is not revealed in the film.

If a double kidney is demonstrated, heminephrectomy is the operation of choice, provided the arrangement of the vascular system permits it. If retrograde pyelography does not determine beyond a doubt to which kidney the ectopic ureter belongs, operative measures will reveal whether, in accordance with Weigert's law, the ureter opening lower down corresponds to the upper pelvis. To obtain this proof, the ureter under suspicion is incised longitudinally, and a catheter is passed from above downward; the point at which the catheter appears at the perineum will then give the site of the ectopic orifice.

Ectopic ureters are particularly prone to be the seat of acute infections which simulate pelvic suppuration of genital origin. Mistaken diagnoses due to this similarity of symptoms have been responsible for many useless laparotomies performed by general surgeons, who have not taken into account the significance of this particular type of incontinence.

Derbes and Dial²⁹ reported 2 cases of postcaval ureter in man, bringing the total number of cases in the literature to 14. Postcaval ureter in man was first described in 1893. Since then 11 cases have been reported.

These authors observed postcaval ureters in 2 adult cadavers. In each case the lower portion of the right renal pelvis and upper portion of the ureter were dilated and thin walled. The ureter passed behind the inferior vena cava at the level of the third lumbar intervertebral disk, at which point it was definitely constricted. It then passed forward between the aorta and the vena cava and thence downward, forward

29. Derbes, V. J., and Dial, W. A.: Postcaval Ureter: Two Cases, *J. Urol.* 36:226-233 (Sept.) 1936.

and laterally across the anterior aspect of the latter vessel. From that point, its course and entrance into the bladder were normal.

In the 14 reported cases, the condition was found in an acardiac fetus, in 2 infants and in 11 adults. Hydronephrosis was present only in the adults, but it was found in all these except 1. In that instance the ureter was encircled by a venous ring at the pelvic brim. It is to be inferred, therefore, that duration is an important factor in the production of hydronephrosis when associated with this anomaly. The hydronephrosis is produced by kinking and stricture attributable to the anomalous course of the ureter, by pressure of the vena cava or by any or all of these factors.

In only 1 of the reported cases was diagnosis of the anomaly made before death, that being made at operation for stone and relief of hydronephrosis. Derbes and Dial stated that they are aware of no way by which a positive preoperative diagnosis can be made, though postcaval ureter should be kept in mind in all cases of hydronephrosis in which the etiology is obscure, as symptoms and sequelae would be similar to those of ureteral obstruction from other causes.

The type of anomaly itself immediately suggests that ureteral dilation or nephropexy will not relieve the hydronephrosis produced by it. If operation becomes necessary and a postcaval ureter is found, a plausible treatment might be transposition of the ureter from its position posterior to the vena cava to an anterior position with ureteropelvic anastomosis.

Calculi.—Grant³⁰ reviewed 100 cases of ureteral stone and arrived at the following conclusions: A large percentage of stones, probably more than 40 per cent, will pass without any treatment except relaxation of the ureter by medicinal means. Another 45 per cent will pass following ureteral manipulation. Ureteral manipulation, even with catheters, is not without danger. Frequently they cause swelling, which may only increase the obstruction, and perhaps, even more often than is suspected, the ureter may be perforated. Perforation below the stone may not cause any grave disturbances. In the case of infected kidneys, when it is possible to introduce a catheter beyond the stone, indwelling catheter and lavage prior to operation are a decided advantage. Likewise, they enable the surgeon to study the function of the kidney and to determine the choice of operative procedure.

Injury.—Wildbolz³¹ proved by an experimental study that if the ends of a ureter which has been cut transversely are properly sutured

30. Grant, Owsley: Cautions in the Treatment of Ureteral Calculi, *Ann. Surg.* 103:935-940 (June) 1936.

31. Wildbolz, Egon: Die quere Ureternaht und ihre Folgen. *Experimentelle Studie, Ztschr. f. urol. Chir. u. Gynäk.* 42:56-79, 1936.

together so that stricture does not occur, the ureter resumes its functions and that the kidney above the anastomosis functions normally. Considerable experimental work has been done on this subject, all of which suggests that hydronephrosis develops above the line of suture. Most of the experimental animals have been killed several days or weeks after operation in order to examine the kidneys, and most of the various investigators have concluded that hydronephrosis was developing because of dilatation of the ureter and pelvis above the line of suture. In most of these experiments the ability of the ureter to hypertrophy had been overlooked.

Wildbolz in his experiments exposed the ureter through a transperitoneal incision, cut it through just below the renal pelvis, resutured the ends together with a circular suture and closed the wound without drainage. This procedure was carried out on 11 dogs. One died the day after operation and 1 a month later. In neither was there infection of the field of operation. A pyelogram was made every six months on the remaining dogs, which were in excellent physical condition. The dogs were killed at the end of two years. In 4 a stricture of the ureter was found at the point of suture, and above that marked hydronephrosis had developed. This hydronephrosis could also be seen in the pyelograms. In 5 dogs good results were obtained. The kidney above the suture was normal, and there was no atrophy of the parenchyma on microscopic examination. The ureter above the suture was dilated, as was also the pelvis in some of the dogs. The wall of the ureter and pelvis was always thickened and the muscularis hypertrophic.

In conclusion, Wildbolz stated that suturing of the transversely cut ureter when properly done does not always cause hydronephrosis. This procedure could readily be used in surgical work in cases in which it is necessary to cut the ureter or it is cut accidentally.

¶ *Transplantation.*—Hinman and his associates,³² from a study of uretero-intestinal implantation, stated that peritonitis rarely occurs as a result of contamination by the contents of the bowel or by urine at the time of operation when obvious precautions are followed. Leakage from the bowel or the ureters after operation is the common cause of peritonitis. Leakage occurs when the anastomosis is faulty and the ureter has not been sutured securely into the opening of the intestine, when anchoring sutures tear or slough out, when a suture punctures the bowel (fecal fistula) or the ureter (urinary fistula) and on necrosis of a portion of the intestine or of the transmural portion of the ureter.

32. Hinman, Frank; Murphy, W. K.; Wyman, Brent; McCorkle, H. J., and Benteen, F. H.: An Experimental Study of Uretero-Intestinal Implantation, Surg., Gynec. & Obst. 62:909-917 (June) 1936.

The blood supply of the bowel or ureter must not be tied off by sutures or impaired by too great constriction, which may occur when suturing is done in layers.

Infection of the abdominal wound from contamination at the time of operation is more likely to result than peritonitis. Abscesses in the abdominal wall may rupture to the inside and produce peritonitis.

Implantation by any method which requires that the bowel be opened at the time carries considerable risk of localized inflammation of both the bowel and the ureter. Localized peritonitis may clear up or become general. An abscess may be absorbed, or it may rupture into the cavity and then produce peritonitis. Periureteritis may produce urinary obstruction, or the infection may ascend to the kidney. Localized inflammation may lead to anemic necrosis of the bowel or ureter, leakage and, ultimately, peritonitis. Inflammation at the site of implantation may result from temporary leakage after operation, and this probably is the most frequent cause.

Counseller³³ has found that the satisfactory results that have been obtained after transplantation of both ureters to the pelvic portion of the colon for exstrophy of the bladder have formed a stimulus for similar surgical treatment of women when the urinary bladder has been rendered useless by traumatism or disease. Counseller in his article refers particularly to huge vesicovaginal fistulas, chronic interstitial cystitis with secondary contraction of the bladder and certain carcinomas of the bladder.

The surgical technic employed follows the principles of C. H. Mayo and Coffey. The right ureter is transplanted first, and the left ureter, not earlier than two weeks later. Thirteen illustrative cases are reviewed briefly. There were three deaths. As the urinary bladder is obviously the best receptacle for urine, bilateral uretero-enterostomy should not be undertaken without serious consideration of all circumstances in each case. Surgical risk is minimized by giving attention to the general condition of the patient; the status of the upper part of the urinary tract, with regard to the presence of obstruction, infection or reduced function of the kidneys; the presence or absence of pelvic cellulitis which involves the lower ends of the ureters; previous surgical procedures on the pelvis, which may have resulted in fixation of the important structures, and the preoperative preparation of the patient. The risk of operation is definitely increased if one attempts to transplant grossly abnormal ureters to the bowel. At times preliminary nephrostomy may be utilized as a procedure to reduce infection and

33. Counseller, V. S.: Bilateral Transplantation of the Ureters of the Female. Proc. Staff Meet., Mayo Clin. 11:699-701 (Oct. 28) 1936.

relieve obstruction to the kidneys prior to ureteral transplantation. Occasionally such a procedure is necessary after treatment of carcinoma of the uterine cervix with radium. Intravenous urography is definitely helpful in determining the status of the kidneys prior to operation.

PROSTATE GLAND

Prostatectomy.—Schanz³⁴ reported 323 new cases in which operation has been performed by Kirschner since 1931. In the total group of 745 cases, there were 574 of adenomatous hypertrophy of the prostate gland. Most of the patients were in poor general health when first seen.

Radical operation was performed on all the patients who were strong enough. Kirschner preferred the perineal route and gave the following reasons for this: When prostatectomy is performed by the suprapubic route, the bladder must be opened twice, and also the prostate gland is situated much deeper than when the perineal approach is employed. The perineal method avoids opening the abdomen and thus diminishes the incidence of pulmonary complications. Bleeding can be controlled easier, and there is no need for a packing. The secretions from the incision drain more readily from the perineal wound than from the suprapubic, and the sphincter muscles can be preserved more readily. In 292 (51 per cent) of Kirschner's cases the perineal route was employed. The mortality was 4.2 per cent, and the results at the time of the patient's dismissal and on reexamination from one to four years later were the best of all methods of treatment. Contraindications to the radical operation are serious disturbances of the circulation or renal function, cachexia, diabetes and perivesical infection.

For the patients who were comparatively well but who could not stand radical operation, suprapubic drainage was instituted. This was the treatment until 1932 and was employed in 94 cases (7 per cent). Since then the patients who could not stand radical operation had been treated by transurethral electroresection; this was used in 42 cases (7 per cent). The great disadvantage of transurethral methods is the risk of leaving a malignant prostate gland without realizing it. Schanz estimated this risk at about 15 per cent. That is the principal reason why Kirschner preferred radical operation. There were 4 deaths (12 per cent) after transurethral electroresection. The results were not as good as those of perineal prostatectomy. The high mortality is due to the fact that all the patients in good general condition underwent prostatectomy.

34. Schanz, F. E.: Ueber Behandlung und Behandlungserfolge des Prostataadenoms, Ztschr. f. urol. Chir. u. Gynäk. 42:169-198, 1936.

One hundred and forty-six patients (26 per cent) were too ill to undergo any operative intervention. For the permanent treatment of inoperable conditions, the indwelling catheter in the urethra is superior to suprapubic drainage. The catheter that is put in after ligation of the vas deferens to prevent epididymitis can be worn for years if properly cared for. Most of the patients on whom suprapubic drainage was instituted were uncomfortable and dissatisfied.

Haim³⁵ stressed the superiority of perineal prostatectomy over all other procedures. He stated that there are only two reasons why it is not used as widely as it deserves: The technic is more difficult, and surgeons who employ the suprapubic method, which is easier to do, are diffident. The advantages of the perineal method are that less shock and fewer cardiac and pulmonary complications result and that there is a reduction in the number of cases of thrombosis and embolism.

To increase the use of perineal prostatectomy, Haim recommended standardizing and simplifying the procedure in order to rule out the possibility of postoperative incontinence and fistulas. These complications occur rarely in the hands of a surgeon skilled in perineal prostatectomy, and when they do occur it is usually in cases of carcinoma. He recommended going in between the anal sphincter and the rectal wall, so that the rectum may be seen during the operation, and the injection of some fluid into the prostate gland between the adenoma and the capsule to make enucleation easier.

Lumb³⁶ reported a technic for suprapubic prostatectomy, its main advantages being the facility with which the floor of the bladder can be reformed and the definite approximation of trigonal tissue to the divided posterior urethra. After an extended trial, this operation has fulfilled its purpose, and its value is enhanced by its simplicity, since complicated instruments and illuminated retractors are not needed for its performance.

Several advantages have resulted from this method: The trigonal flap is stretched evenly over as large a portion of the posterior aspect of the prostatic cavity as it can be made to cover. There is maximal approximation of the trigon to the posterior urethra, intimate contact between the whole of the trigonal flap and the underlying wall of the prostatic cavity and reduction of hemorrhage. The floor of the bladder, when reformed, closely approximates normal.

A gum elastic coude catheter having two eyes is threaded with two moderately stout silk threads about 18 inches (46 cm.) long, so

35. Haim, Emil: Gedanken zur Behandlung der Prostatahypertrophie, *Wien. med. Wchnschr.* 86:1004-1007 (Sept. 5) 1936.

36. Lumb, Norman: Trigonal Loop-Traction in Suprapubic Prostatectomy. *Brit. J. Urol.* 8:257-265 (Sept.) 1936.

arranged that about 3 inches (7.6 cm.) of each projects from each eye. The catheter is passed into the bladder, and the distending fluid is injected. A wooden spigot closes the catheter, and a sterile towel is arranged on which the outer ends of the silk threads rest beside the catheter. A pair of small artery forceps is attached to one thread and a pair of large forceps to the other, so that the threads may be distinguished subsequently, or silk threads of different color may be used.

A midline incision is preferred, though a transverse one may be adopted equally well; the peritoneum is displaced gently upward, exposing the bladder, which is opened at its highest point. The wall of the bladder is punctured, and a suction tube is used to evacuate the contents. Great care is taken to avoid opening the cellular tissue in front of the bladder.

The ends of the two silk threads which are in the bladder are unthreaded from the eye of the catheter; a small forceps is placed on one and a large forceps on the other, and the catheter is withdrawn. Two separate silk threads thus traverse the urethra from the meatus to the bladder. The prostate is enucleated as expeditiously as possible. Dry gauze from a 3 inch roll is lightly packed into the cavity to check hemorrhage. A self-retaining retractor is inserted, and the gauze is withdrawn.

A fine silk suture, 18 inches long, is made through the trigon in the middle line, about $\frac{1}{2}$ inch (1.3 cm.) behind the raw edge, thus securing a firm hold on it. The ends of the suture material are tied to the bladder end of one of the silk threads previously mentioned and drawn through the urethra to the external meatus. When the threads are pulled tight a triangular flap of trigon is drawn down, largely obliterating the posterior portion of the prostatic cavity and diminishing the bleeding. The weight of the forceps attached to the silk thread will be found sufficient to keep the flap in position at this stage, and the indwelling catheter is inserted next. A flute-ended india rubber catheter, size 22, with two lateral openings, is used for this purpose. After lubrication it is readily drawn into the bladder by the second silk thread, which is secured to its tip. The silk thread is removed, and a stout silkworm gut stitch is attached instead to the tip of the catheter, the ends being held in a forceps. This is used later for suspending the catheter in its final position within the bladder.

At this stage bleeding is considerably diminished, and the remainder of the plastic portion of the operation consists in inserting the anterior obliterating stitches. These may be made more effective by using the infolding method to be described, as they then tend to diminish pocketing in the anterior part of the cavity during healing. A wide hold is

taken with the boomerang needle, and the catgut stitch is drawn through. The two free ends of catgut are made to cross to opposite sides of the prostatic cavity, where each is threaded on a needle, a portion of the rim is picked up and the ends emerge once more into the bladder. On tying the ends, infolding takes place and the edges are well inverted.

The catheter is carefully adjusted so that its lower lateral eye lies just at the entrance to the torn posterior urethra, thus draining the prostatic cavity completely, and a small drainage tube is placed in the bladder. Closure of the wound in the bladder is carried out in the usual way, with an inverting stitch, followed by a second layer of fine catgut. The drainage tube should lie at the upper end of the incision into the bladder and be firmly gripped; the loop of silkworm gut suspending the catheter emerges immediately below it. The catheter is left in place for from ten to twelve days and then removed, together with the traction stitch from the trigon.

Resection.—Thompson and Buchtel³⁷ reported a series of 200 consecutive cases of prostatic hypertrophy in which treatment involved transurethral resection of 25 Gm. or more of prostatic tissue; 140 patients, or 70 per cent, had suffered from complete urinary retention. Eighty-eight patients, or 44 per cent, were aged 70 years or more.

Thorough removal of all adenomatous tissue which encroaches on the neck of the bladder, particularly in the anterior half, so that all inverted V deformity is eliminated, and careful hemostasis during the progress of the operation are important points in technic. An operation must not be prolonged or shock may result; in Thompson and Buchtel's experience, patients withstand a two stage or three stage procedure, each of short duration, much better than a single operation which lasts more than one hour. The bladder must not be allowed to become over-distended at any time during operation or during the postoperative course or fever may ensue. If the functional result is not good immediately after drainage by inlying catheter has been discontinued, judicious intermittent catheterization or early reoperation is essential to an uncomplicated convalescence.

Replies to letters of inquiry indicate a high degree of satisfaction among the patients. Sixteen patients (15 with benign lesions and 1 with a malignant lesion) have returned to the clinic for reoperation six months or more after their dismissal. One of these patients was subjected to perineal prostatectomy, while the others preferred to undergo further transurethral resection. The mortality in the series was 1.5 per cent.

37. Thompson, G. J., and Buchtel, Henry: Transurethral Resection of the Large Prostate: Review of Two Hundred Cases in Which Twenty-Five Grams or More of Tissue Was Removed, *J. Urol.* **36**:43-56 (July) 1936.

It occurred to Emmett³⁸ that because of the hemostatic quality of posterior pituitary it might be of value in the reduction of hemorrhage in transurethral resection of the prostate gland. Resection at the Mayo Clinic is performed by means of the direct vision, cold-cutting resectoscope, in which an electric current is employed only to fulgurate individual bleeding points after tissue has been removed by the tubular knife. Because of the fact that a lens system is not employed, bleeding causes little difficulty with vision. However, it is important that as little blood as possible be lost during and after the operation; hence, any method that might aid in conservation of blood is worthy of investigation.

A rigid needle has been constructed, with a shaft long enough to project through the full length of a Braasch direct vision cystoscope. The needle proper is of 21 gage and is $\frac{7}{8}$ inch (2 cm.) in length; it has a small, circular hilt where it joins the shaft to prevent it from being inserted any farther than its length into the prostatic tissue. At operation an injection is made into each of the three prostatic lobes. To make the injection, the heel of the cystoscope is placed against the portion of the lobe into which the solution of posterior pituitary is to be injected, and the cystoscope is maneuvered so that it forms, as nearly as possible, a right angle with the surface of the lobe. This is done in order to assure the injection of material well into the tissue rather than just having the needle slide under the mucosa. This is the most difficult part of the technic of the injection. The needle is then introduced blindly, as one implants radon seeds, and is inserted into prostatic tissue to the hilt. A third of the total dose of posterior pituitary is injected into each lobe. A total injection of from 1 to 3 cc. of solution of posterior pituitary of double U. S. P. strength has been used, but 2 cc. seems to be about the proper amount. In 2 cases a mixture of 1 cc. of solution of posterior pituitary and 1 cc. of ergotamine tartrate was used.

In 31 consecutive cases in which resection of the prostate gland was performed, the foregoing method of injection was employed. Spinal anesthesia was used in all the cases. In 29 cases injections of solution of posterior pituitary alone were given, the total dose varying from 1 to 3 cc., whereas in 2, injection of a combination of 1 cc. of solution of posterior pituitary and 1 cc. of ergotamine tartrate was employed.

Results of injection are interesting. In 25 cases results were satisfactory; in 7 of these no bleeding was encountered at the operation,

38. Emmett, J. L.: Preoperative Intraprostatic Injection of Pituitrin in Transurethral Resection: Preliminary Report, Proc. Staff Meet., Mayo Clin. **11**: 619-622 (Sept. 23) 1936.

which was terminated within thirty or thirty-five minutes. In the remaining 18 cases the wash water was colorless for periods varying from twenty-two to forty-seven minutes. The average length of time for the water to remain clear was about twenty-seven minutes. In these cases, after this period vessels began to bleed in varying degrees from slight to rather sharp bleeding. All bleeding was easily controlled with the usual fulguration. In the remaining 6 cases, experience in which was not classed as satisfactory, the results were as follows: In 2 they were fair; that is, at no period was the wash water absolutely colorless, but instead it was only a light pink for about twenty to twenty-five minutes, after which the usual bleeding occurred; in 1 of the remaining 4 the wash water was colorless for ten minutes, and then moderate bleeding occurred, while in the other 3 it was difficult to say whether the posterior pituitary had any effect.

Kretschmer³⁹ stated that his position in the discussion of transurethral resection can best be summarized by saying that during the past fifty-one months he performed prostatectomy only once and that during the same time he refused resection to only 1 patient.

The period of hospitalization is much shorter with resection than it is with surgical prostatectomy, and while this fact may not be of much importance to a small percentage of patients, all things being equal, it is an economic factor of enough importance to demand attention.

The number of cases in which preliminary suprapubic cystostomy is employed has become fewer and fewer. During the past three months preliminary cystostomy has been done only once. On the other hand, Kretschmer expressed the belief that cystostomy is indicated when drainage by catheter fails because of chills, fever, pain or bleeding, or when small stones with severe infection or large stones are present.

The number of patients with cardiac conditions seeking relief has increased definitely. Whereas, in the days of surgical prostatectomy about 35.8 per cent of the patients suffered from cardiovascular lesions, a recent study of Kretschmer's cases in which resection was performed revealed cardiovascular lesions in 64.3 per cent, an increase of 28.5 per cent.

As Kretschmer's experience with resection widened, he performed operation in a certain group of cases without preliminary drainage by catheter. Heretofore all patients who had 4 ounces or more (120 cc.) of residual urine were given preliminary drainage. At present no preliminary drainage is employed in a case in which the residual urine does not exceed 6 ounces (180 cc.), provided the urine is clear, the

39. Kretschmer, H. L.: Transurethral Resection, *Ann. Surg.* **104**:917-933 (Nov.) 1936.

renal function normal and the heart and lungs in good condition. Preliminary cystoscopy is no longer carried out as a routine; once the diagnosis of prostatic obstruction has been made, the type of enlargement is determined when resection is performed. The exceptions to this rule are: in case the history is not typical for prostatic obstruction, if there is a history of one or more attacks of hematuria and if the cystogram reveals a filling defect.

In Kretschmer's series of cases in which resection was done, a second resection was performed in 10.6 per cent and a third one in 3.7 per cent.

Before the technic of resection was completely mastered, hemorrhage at operation was at times a serious problem, but with experience this untoward occurrence has become less of a problem, although occasionally a serious hemorrhage occurs no matter how careful one is. Careful search for the bleeding point should be made and its immediate control effected. Secondary bleeding, which was never severe, occurred in 19 cases on the tenth to the fourteenth day. Clots, when present, were evacuated with the Bigelow pump, and the bladder was washed out with a warm solution of silver nitrate. In most of the cases this controlled the bleeding, but when this procedure failed the resectoscope was introduced, and the bleeding point was fulgurated or excised. Late hemorrhage occurred in 14 cases at periods varying from three months to two years after resection. In the patients who were reexamined, enlarged vessels were found around the orifice of the bladder and in the prostatic urethra. These were destroyed by fulguration. An interesting fact is that these late hemorrhages occurred in patients with large prostate glands.

The incidence of epididymitis has diminished as experience with resection has grown. In 15 per cent of the first 117 cases this complication occurred, and vasectomy was done as a routine, an operation no longer employed, as this complication is very rare.

There has been no instance of complete incontinence in Kretschmer's series of 804 cases in which resection was performed. Shortly after leaving the hospital a small number of patients have had difficulty in holding urine. This was due not to incontinence but to urgency and imperative urination. Continence of urine was eventually recovered. In a few instances the patients would lose a few drops, but this was temporary, and as the infection cleared up the condition rapidly disappeared. In 2 instances the loss of a few drops of urine was due not to incontinence but to stricture of the urethra.

The mortality has fluctuated from time to time, depending in part on the type of cases and whether or not one wishes to refuse resection to many of the patients who are considered bad risks, which Kretschmer

has not done. His records show that he has performed 184 resections with but 1 death—a mortality of 0.54 per cent. The 804 patients who were operated on included a large number who were classed as bad risks, and the mortality for the entire series was 3.9 per cent.

Beer⁴⁰ stated that these new methods of transurethral resection are of use in the following conditions:

1. Contractures of the neck of the bladder, which in years past were excised by a wedge-shaped excision from above through the bladder. These can be cut with a point or loop electrode, an ordinary operating cystoscope or a resectoscope being used. Complete relief from symptoms results. This is a great improvement over the cold punch operation or the suprapubic excision. The latter procedure or approach, however, may be useful when the exact physical status of the neck of the bladder is not accurately visualized.

2. Obstruction caused by carcinoma of the prostate gland. This condition also lends itself satisfactorily to transurethral resection, which may be repeated as a new obstruction develops. The tissue removed during such an operation is often helpful in establishing the correct diagnosis.

3. The ordinary and usual type of prostatic hypertrophy or adenoma. When it comes to these conditions the field of transurethral resection has no limitations for some enthusiasts and definite limitations for others. Included here as a subgroup is moderate prostatic enlargement associated with mild symptoms of frequency and questionable obstruction and a small amount of residual urine. No experienced surgeon would feel justified in performing prostatectomy on a patient with a condition of this type. Such patients present a definite potential field for transurethral resection and may represent a large proportion of the total in most published series of resections. The frequency, and perhaps the infection, do not always disappear but may be made worse after excision of some prostatic tissue, despite a reduction of the residual urine. In these cases the lesion is definitely a beginning prostatic adenoma and is not to be considered with those cases in which prophylactic resection has been performed before any definite complaint has developed. It is doubtful whether resection affords the patient the expected relief with any regularity. If the subjective complaints are well developed, one is justified in attempting to give relief by resection, even though it may be only temporary and incomplete. Correct diagnosis here, as always, is essential.

In addition to those patients with mild symptoms referable to the prostate gland who frequently are worse off after resection, there are

40. Beer, Edwin, in discussion on Kretschmer,³⁹ pp. 928-931.

two other groups of patients who have definite prostatic adenoma that must be discussed: those with moderately large, bilobed, trilobed or single lobed prostate, and those with large, more or less trilobed or bilobed hypertrophy. In localities in which no pressure is brought to bear on the surgeon by competitors, the patient or his friends, the opinion is gradually developing that the last-mentioned group, with large, succulent adenomas, should be treated radically and definitively by prostatectomy or enucleation of the adenoma, either by the suprapubic or by the perineal approach. This attitude seems to be based on a great many factors, without denying that if the "resectionist" is patient he can whittle away a fair amount of the largest prostate in one or more sessions.

The two stage suprapubic prostatectomy has gradually assumed the status of an almost minor procedure, with a low mortality, of 6 + per cent, which is usually incidental to cardiovascular disturbances, and with complete cure without chance of recurrence, if properly performed. On the other hand, the transurethral approach for the large adenoma frequently is followed by a whole group of complications, such as primary or secondary hemorrhage into the bladder, which necessitates repeated evacuation of clots, infection of the bladder and more or less complete resection of the base of the prostate gland which frequently, much more frequently than is reported, may turn the scales against the patient, not to mention the various instrumental damages and perforations that are reported by competent instrumentalists. Because of the prolongation of the necessary instrumental work and the various complications, the mortality is likely to be definitely higher than with the transurethral approach with a two stage suprapubic enucleation. This is Beer's experience. He stated that if the statistics on prostatic adenoma alone were considered, the data of other clinics would probably bear him out. The trouble with most statistical studies along these lines is that they include the results of operation for simple contracture, small, almost symptomless hypertrophy and moderate-sized but definite adenoma of the prostate gland as well as extensive hypertrophy and of prophylactic excisions, done perhaps because of incorrect interpretation cystoscopically.

In the moderately enlarged prostates, as opposed to the very large adenomas, which weigh an ounce (28 Gm.) or more and are as large as one to three or more lemons, there is a definite field of usefulness for transurethral resection, even though repeated sessions may be required before the patient can void and be comfortable and even though, as time goes on, one may see more and more of these partially removed adenomas redevelop and produce recurring symptoms, which is a rare sequela to a properly executed complete enucleation. There is no doubt

that in this group of moderately enlarged prostates one is justified in using transurethral resection, if the patient requests it and especially if he is a poor surgical risk because of poor renal function, coronary disease, diabetes, etc.

According to Beer, a careful follow-up of the cases in which resection was done leaves much to be desired.

Beer stated that he was impressed by the reports of large numbers of cases in which resection has been performed and yet continued treatment, soundings, irrigations of the bladder, etc., are necessary; these are practically never required when a proper prostatectomy has been performed. There is no doubt that most patients void more readily after resection and have much less residual urine than before the operation, but a large number of patients are not absolutely and definitely cured, as they are after a complete enucleation of the adenoma. Pyuria, frequency and dysuria often persist for months or permanently in every series of cases in which a really careful check is maintained.

That transurethral resection of the prostate gland has become an unusually popular procedure, without due selection of cases, cannot be denied.

Lower⁴¹ stated that transurethral resection of the neck of the bladder for obstruction has been revived in the last few years, probably because of improvements in instruments and electrical apparatus. Not only are the median bars and the sclerotic obstructions resected now, but the use of transurethral resection is being extended to include a much wider field, especially in the treatment of prostatic hypertrophy.

In what cases should this procedure be used? Experience has taught that its scope of usefulness is much wider than was formerly thought, but again the danger of broadcasting the simplicity of the operation should be emphasized. However, it is true that it carries with it a low mortality, and so far the postoperative results in most cases have been good. Among approximately 500 resections which have been performed at Lower's Clinic, the mortality has been 1.8 per cent, including a series of 225 cases in which no deaths occurred. These were not selected cases, but included all types. Among the patients were many feeble and elderly persons.

As wider experience has been gained, larger and larger amounts of tissue have been removed. Another advantage of this operation is that a second or even a third operation may be performed if necessary without any special risk.

Bleeding is becoming inconsequential. When the procedure was first used, bleeding occurred frequently, but Lower has found it necessary to open the bladder in only 1 case.

41. Lower, W. E., in discussion on Kretschmer,³⁹ pp. 931-932.

The incidence of epididymitis in the entire series was 6.8 per cent, and the average stay in the hospital was less than seven days; this economic factor is of considerable importance, especially in these times.

Cabot⁴² stated that in the first place there are various methods of whittling out the prostate through the urethra. His notion is that the instruments will probably be greatly modified. The problem should be discussed without prejudice. Beer has perhaps a case to prove; he performs chiefly prostatectomy. Kretschmer has a case to prove; he does chiefly resection. Cabot stated that he has no case to prove.

In reference to Beer's remarks on the unfortunate results of resection, Cabot stated that if the truth were told, the statistics would be loaded handsomely with the unfortunate results of prostatectomy. The mortality of prostatectomy, which up to the last few years was over 50 per cent in the hands of the occasional surgeon, has never been less than 20 per cent the country over, and is not now. Prostatectomy is an operation for experts, whether the suprapubic, the transurethral or the perineal method is used. The discussions should be confined to the results obtained by experts, not to the results obtained by surgeons who operate on the patient not for prostatic obstruction but for a hundred dollars. That will cause damage, and does, in every field of surgery. It is not fair to the operation.

Six years ago, more than half the patients on Cabot's surgical list were to have prostatectomies, but he has not done a prostatectomy in three years. There have been only 3 or 4 done in the last two years at the Mayo Clinic.

The age group is interesting. Of 1,922 consecutive prostatectomies done between 1924 and 1932, 5.6 per cent were performed on patients more than 75 years of age. Of the last 700 transurethral resections done up to Jan. 1, 1936, 15.7 per cent were performed on patients over 75.

It is frequently suggested that this operation is being performed chiefly for patients who do not need it, which is not entirely true. Patients who are more gravely ill are being operated on with better results.

It has been the habit at the Mayo Clinic, and it is not a bad one, to keep all the tissue which the surgeon removes. About a year ago Cabot thought that it would be interesting in a series of 1,000 cases to take a fair average of the gross amount of prostatic tissue removed by suprapubic prostatectomy and to compare it with the gross amount removed by transurethral resection. The amounts removed by resection are approaching those removed by prostatectomy. The group of men at the Mayo Clinic who perform resections now take out almost as

42. Cabot, Hugh, in discussion on Kretschmer,³⁹ p. 932.

much tissue on the average as was taken out by prostatectomy five years ago. It thus appears that the transurethral route is becoming the method of prostatectomy. If the same amount of skill for this method is insisted on as is shown by the experts using the suprapubic or the perineal route, resection has much to offer and will cover a large portion of the field.

Carcinoma.—Chauvin and Mosinger⁴³ asserted that the histogenesis of malpighian tumors of the prostate and other viscera which, like the prostate, possess no paramalpighian structure, is a subject of the greatest interest and that three hypotheses have been suggested to account for it. 1. The tumor develops on an island of malpighian metaplasia, such as can be observed in the biliary and respiratory tracts and in the body of the uterus after a chronic inflammatory process. 2. The tumor develops on a dysembryoplastic soil. 3. It is the result of the direct transformation of normal epithelium into a cancerous tissue of malpighian structure.

In order to choose among these hypotheses, the authors undertook to discover the relative frequency of malpighian or paramalpighian islands in nontumorous prostates, in adenomas of the prostate and in epitheliomas in which glandular substance predominates. In a malpighian epithelioma of the prostate they found an adenomatous zone and an epitheliomatous zone, the latter in the center of the former. They were thus able to prove the coexistence of an adenomyoma of the prostate in which the hyperplastic process was doubled by the phenomenon of malpighian metaplasia and a malpighian epithelioma grafted on the adenomyoma.

It might have been thought, in view of the frequency of a malpighian metaplastic process in the purely adenomatous zone, that the epithelioma developed from a malpighian island. But a study of the epitheliomatous zone revealed conclusively that metaplastic malpighian trabeculae could arise directly from epithelial tubes that were themselves tumorous. Chauvin and Mosinger were able to demonstrate beyond a doubt the truth of the third hypothesis, that of immediate tumor metaplasia; but that this process occurs in a predisposed territory was shown by the frequency of metaplastic islands disseminated in the adenomatous zone. In nontumorous prostates in which there was chronic prostatitis, they found islands of malpighian metaplasia developing often in contact with islands of inflammatory connective tissue. Of 6 prostatic epitheliomas of various structures, they observed malpighian islands lying in the midst of the tumor tissue in 3.

43. Chauvin, E., and Mosinger, M.: Sur les épithéliomas malpighiens de la prostate et leur histogénèse, *J. d'urolog.* 41:297-306 (April) 1936.

They concluded that malpighian metaplasia is observed in 32 per cent of cases of adenoma of the prostate and in an equal percentage of cases of prostatitis. The possibility of malpighian cancers developing secondarily from these islands must then be faced. However, the study of their own case of malpighian cancer and the frequency of malpighian islands in cancers of the prostate of different structure show that the malpighian aspect may appear even at the moment of canceration.

Uebelhör⁴⁴ stated that fairly uniform results are obtained in most clinics in the treatment of carcinoma of the prostate; namely, only a few lasting cures are obtained, but there is improvement in many cases.

The first question that Uebelhör discussed is: Why do so few surgeons use the perineal method, when Young and Wildbolz get such good results? The answer is easy; most surgeons use the suprapubic approach as a routine procedure, and when they perform perineal prostatectomy occasionally for carcinoma they have a great percentage of fistulas, incontinence and strictures, which discredits the method in their eyes. Uebelhör and the representatives of the Viennese school prefer the suprapubic route for prostatectomy, but Uebelhör expressed the belief that it would be wise to practice the perineal method also in order to be able to use it with success in suitable cases.

Radical operations have not found many followers. The shock to the patients is too great, and the chances of freedom from cancer are too unstable. Suprapubic drainage is not "the best of all methods" in these cases, as has often been quoted. Its use is justified only in cases of obstruction, in which it is competing successfully with transurethral resection. Uebelhör stated that roentgen therapy according to the Coutard technic or radium therapy in combination with surgical intervention is the most promising method. The remarkable variations in the course of the disease make estimation of the value of any new method of treatment difficult; for example, occasional patients survive more than four years after a definite diagnosis of carcinoma has been made, even in the absence of treatment.

Keyes and Ferguson⁴⁵ argued that the term "early" as applied to prostatic carcinoma covers that group of cases in which diagnosis cannot be made by rectal examination. The disease surely exists before it is palpable by rectum. There have been cures when the malignant growth was confined to a hypertrophied portion of the gland and the patient was fortunate enough to have undergone prostatectomy for the relief of the enlargement. The carcinoma, not having extended to the remain-

44. Uebelhör, Richard: *Bemerkungen zur Therapie des Prostatakarzinoms*, Wien. med. Wchnschr. 86:1038-1044 (Sept. 5) 1936.

45. Keyes, E. L., and Ferguson, R. S.: *Early Diagnosis and Radical Treatment of Carcinoma of the Prostate*, Brit. J. Urol. 8:346-352 (Dec.) 1936.

der of the gland, comes out with the adenoma, and its presence is unsuspected until shown on pathologic section.

Because of the difficulties of recognition of this "early" prostatic carcinoma, Keyes and Ferguson removed material for biopsy by aspiration from all prostates in men aged more than 50 years whose glands were the least bit irregular. They reported on 2 series of cases in which biopsy specimens were secured in this manner. In the first series, consisting of 100 cases, biopsy was done by Ferguson at the Memorial Hospital. In 18 of the cases insufficient tissue was obtained to permit a diagnosis. In 59 of the others a diagnosis of carcinoma was made, and in 23 the tissue was found to be noncarcinomatous. Fifty-seven patients in whose prostates carcinoma was found have died of carcinoma. One of the survivors is living, but metastasis has occurred, and the other, who submitted to interstitial irradiation by the Ferguson technic, is alive and well. Those patients whose tissue was pronounced to be noncarcinomatous have remained free from the disease to date.

In a similar series of 33 cases in which tyros undertook to perform biopsy on specimens obtained by aspiration, no tissue or insufficient tissue was obtained in the first 14 cases, and the pathologist was not able to distinguish carcinoma until the twenty-fourth specimen. After that he found tumor cells in 10 cases in succession. As in the first series, in no case in which the specimen was reported as noncarcinomatous are symptoms of carcinoma of the prostate known to have developed.

The method employed by the authors for the radical treatment of carcinoma of the prostate is the implantation of gold radon seeds (each containing 2 millicuries of the radium emanation) into the tumor by means of an instrument devised by Ferguson. This permits the accurate placing of the seeds, the urethral and vesical mucosa and the normal tissues about the tumor being avoided.

Since first using this method in May 1931, Ferguson has studied 41 patients treated by his technic by himself and others. He groups them according to results as follows: "rectal touch doubtful, biopsy positive," 14 patients, 9 of whom are alive and well, 4 for more than three years; "touch and biopsy both positive," 27 patients, 4 of whom are alive and well from one to two years. The authors stated that this procedure, with its low mortality, promises to compare favorably with the total prostatectomy of Young.

Nitch⁴⁶ stated that conservative treatment of carcinoma of the prostate comprises radiotherapy, surgical procedures and surgical procedures combined with radiotherapy.

46. Nitch, C. A. R.: *The Conservative Treatment of Carcinoma of the Prostate*, Kong. d. internat. Gesellsch. f. Urol. **6**:147-154 (Sept.) 1936.

The immediate results of roentgen treatment are often excellent, but the ultimate results are disappointing. In some cases the roentgen rays cause a rapid increase of the growth and dissemination. The best results are obtained by the five field maximal method of Holfelder-Reisner with a total depth dose of from 150 to 200 per cent on the prostate. The intensive split dose method of Levitt, now under trial, seems productive of better results. At present only 6 per cent of cures can be claimed for modern methods of roentgen therapy. The results of radium therapy are better, especially when applied in large doses to the rectal, vesical and urethral surfaces of the prostate. Before treatment is begun, a thorough clinical, biochemical and roentgenographic examination must be made, and a portion of the prostate should be removed by electroresection for microscopic examination. About 70 mg. of radium is used in the treatment as follows: Fourteen milligrams is applied to the posterolateral surfaces, 50 mg. to the vesical surface and 5 mg. to the urethral surface. Though only a few patients have been treated in this way, the percentage of cures has been 28 up to the present. The method is therefore worthy of an extended trial. When results of renal function tests are below normal, preliminary drainage of the bladder is necessary.

Conservative surgical treatment consists of suprapubic drainage, transplantation of the ureters and electroresection. Transplantation of the ureters into the large intestine is preferable to suprapubic drainage but can be performed only in carefully selected cases.

Electroresection is the best palliative measure for the relief of obstruction caused by growth at the neck of the bladder. It is of no value when the obstruction is due to invasion of the prostatic urethra. It is probable that in the future electroresection followed by some form of radiotherapy will be the method of choice in treatment of carcinoma of the prostate.

Schanz⁴⁷ recorded Kirschner's experience of nineteen years in the treatment of diseases of the prostate in surgical clinics of Königsberg, Tübingen and Heidelberg and reported the results of surgical treatment in 144 cases of prostatic carcinoma. He stated that the radical perineal operation is the ideal treatment for a prostatic malignant condition and is the only method that offers a possibility of permanent cure. Operation is performed only when the patient is in good general condition and when the growth has not extended beyond the prostatic capsule. Under these circumstances the difficulties of the operation are not too great, and there is hope of complete elimination of all the tumor

47. Schanz, F. E.: Prostatakrebs, *Ztschr. f. urol. Chir. u. Gynäk.* **42**:292-307, 1936.

tissue. In the early stage of the disease radical operation is superior to any type of treatment. Surgical removal of the gland is usually followed by roentgen therapy.

Patients who do not present these ideal conditions for operation are usually treated by transurethral electroresection of sufficient extent to relieve urinary obstruction. The advantage of a free flow of urine is more important than the danger of a rapid increase in the growth of the prostate. Patients who are unable to undergo even prostatic resection are treated by an indwelling urethral catheter. Suprapubic drainage was instituted only in the cases in which none of these procedures were possible.

Leiomyoma.—Baretz⁴⁸ reported a case of leiomyoma of the prostate gland, making a total of 13 cases of this rare lesion reported in the literature. This type of neoplasm cannot be diagnosed clinically, but it should be borne in mind when a prostate gland, on palpation, is firm, elastic or somewhat unusual in consistence. The growth is benign, and it produces symptoms similar to those of benign hypertrophy of the prostate gland except for increased rectal symptoms. It can be distinguished from benign hyperplasia or sarcoma only by histologic study. It may involve only a small portion of the gland or may have entirely replaced it.

Cysts.—Emmett and Braasch⁴⁹ stated that the most common cyst of the prostate gland is the simple retention cyst. This type of cyst is probably produced by obstruction to drainage of the normal prostatic acini with subsequent dilatation or by the coalescing of smaller cysts by means of rupture of the wall of an adjacent cyst. Small symptomless prostatic cysts, which are 0.5 cm. in diameter or smaller, are rather common. Most prostatic cysts never produce symptoms. Emmett and Braasch collected all cases of prostatic cyst reported in the literature since 1925 and summarized them. A series of 14 cases is reported in which prostatic cysts 0.75 cm. in diameter or larger have been encountered.

Diverticulitis.—Heitz-Boyer,⁵⁰ on the basis of a complicated case, demonstrated the value of cystography and urethrography in the diagnosis and treatment of severe diverticulitis of the prostate gland.

48. Baretz, L. H.: *Leiomyoma of the Prostate*, J. Urol. **35**:664-667 (June) 1936.

49. Emmett, J. L., and Braasch, W. F.: *Cysts of the Prostate Gland*, J. Urol. **36**:236-249 (Sept.) 1936.

50. Heitz-Boyer, M.: *Observation type d'un cas complexe de maladie diverticulaire, à forme de prostatite chronique hypertrophianta; avec opération et guérison des multiples accidents*, J. d'Urol. **41**:369-387 (April) 1936.

Intense chronic inflammation of the entire prostatic urethra was present, and manifestations of peridiverticulitis leading to chronic prostatitis had been superimposed. The prostatitis was of both the sclerotic and the hypertrophic type and caused the patient to drag out a miserable existence. Urethroscopy revealed the orifice of the diverticulum, rather high up and at the left of the verumontanum; from this opening fibrinous agglomerations, a sort of "diverticular expectoration," were expelled from time to time. Above the verumontanum there was a depression forming a kind of "grotto." Cystoscopy revealed stenosis of the neck of the bladder with a columnar effect, numerous depressions appearing between the columns, while the two urethral orifices were widely dilated. As a result of this complex pathologic condition, retention of urine had caused dilatation of the kidneys, the pelvis of which were two or three times normal size, and colon bacilli were present.

Endo-urethral treatment was carried out, consisting first of the exenteration of the diverticulum and the establishment of a wide communication in the prostatic cavity, after which the neck of the bladder was resected. As a result of operation the patient now urinates normally, there is no residual urine and the exaggerated contractility of the muscle of the bladder and the stenosis of the neck of the bladder have disappeared. The vesicoprostatic junction has been reestablished in its proper funnel shape. The patient is cured functionally as well as anatomically. Heitz-Boyer felt that such a result is a clear demonstration of the value of modern urethroscopic and transurethral treatment.

Intraprostatic Injection.—O'Connor and Ladd⁵¹ reviewed the literature dealing with the clinical procedure of direct injection of medicinal solutions into the prostate gland. All previous authors on this subject have inferred that the rationale of the procedure is based on the direct bactericidal effect of the injected solution for the organisms retained in the prostatic acini and ducts. Encouraging clinical reports on intraprostatic injection of solutions in cases of chronic prostatitis have recently extended and revived the interest in this subject. A careful survey of all these reports failed to reveal any published work in which data were given to show what tissue changes actually occur in animals when these solutions have been injected directly into the prostate gland. The experimental work presented by O'Connor and Ladd demonstrated the effects of simple needling of the dog's prostate gland, the changes after the injection of sterile physiologic solution of sodium chloride, distilled water and solutions of mercurochrome, silvol, metaphen, merxyl, merthiolate and electrargol (a colloidal suspension of silver).

51. O'Connor, V. J., and Ladd, R. L.: Intraprostatic Injection: An Experimental Study, J. A. M. A. **107**:1185-1188 (Oct. 10) 1936.

The technic of injection was devised to avoid all trauma, and the glands were removed en masse after periods varying from two days to three months.

O'Connor and Ladd concluded that the trauma of simple needling of the normal dog's prostate gland is followed by an inflammatory reaction, with considerable subsequent fibrosis and glandular destruction. All the solutions injected into the prostate glands of a series of 31 dogs brought about relatively uniform changes. These changes varied only in severity and degree. It would appear from these studies that any solution injected into the prostate, whether it is physiologic solution of sodium chloride, distilled water or solution of a so-called antiseptic character, results in marked destruction of the acini, chronic inflammatory changes and marked fibrosis. The clinical benefit reported after this procedure might be attributed more properly to fibrotic replacement of infected glandular areas than to an immediate antiseptic effect at the time of injection.

(To be continued)

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ORIGIN OF FETAL ADENOMA IN THE THYROID GLAND

WALLACE B. MURPHY, M.D.

Clinical Assistant Visiting Surgeon, Bellevue Hospital; Instructor in
Surgery, New York University

AND

GERHARD AHNQUIST, M.D.

NEW YORK

The term "fetal adenoma" has long occupied a place in the literature on the thyroid gland. The first use of this term is generally credited to Wölfler,¹ who in 1883 used it to designate certain nodular tumors of the thyroid gland, which he thought arose from fetal cell rests. With an advance in knowledge, however, the concept of a fetal origin for these nodules has largely been discarded, although through usage the term persists in the literature. Today it has come to designate a distinctive type of nodule, on the general features of which most observers are agreed.

While a detailed description of a typical "fetal adenoma" will be given later (fig. 1), a few of its distinctive features may be cited here. Such a nodule is discrete, circumscribed, encapsulated and of variable size, occurring alone or multiply and presenting to the unaided eye a dull gray homogeneous substance with no evidence of lobulation. Histologically, it is comprised of small groups of cells, with or without acini, that may have a uniform distribution or show a tendency to congregate toward the periphery of the nodule. The acini are embedded in a homogeneous, eosinophilic, acellular matrix, not unlike colloid in its staining reactions, which is characteristically lacking in connective tissue. The nodule usually has a rich capillary blood supply.

Wölfler noted the occurrence of circumscribed areas in the thyroid gland "varying in size from that of the head of a pin to that of a goose egg." Variations in color and consistency were noted. Some glands contained more than one "adenoma." Microscopically, the smaller nodules were "formed of nonorganized gland cell tissue" and

From the Department of Pathology, and the Third Surgical Division (New York University Medical College, Graduate Course in Surgery) of Bellevue Hospital.

1. Wölfler, A.: Ueber die Entwicklung und den Bau des Kropfes, Arch. f. klin. Chir. 29:1-97, 1883.

"looked like the embryonic thyroid." In his material it was rare to find the "formation of large vesicles or extensive colloid degeneration." Without knowing the etiology and pathogenesis of an adenoma of the thyroid gland, he stated "with some sureness that they are of congenital nature," and more specifically, that they arise from interacinar cell rests. He further added that "these adenomas have a perceptible size at time of birth" or that "they develop at the time of puberty or pregnancy out of congenital structures."

Wölfler's concepts as recorded by his descriptions and diagrams have some features which suggest that he was dealing with nodules of different types and even with true benign neoplasms. Technical improvements in the microscopic examination of tissues, notably examination of whole glands and serial sections, have disclosed certain erroneous deductions in the investigations of earlier workers. The uncertainty of Wölfler's observations and their interpretation makes appraisal of his views impracticable. Nevertheless, he represents the school which originally sponsored the fetal origin of this condition.

Beck,² even earlier than Wölfler, attributed a fetal origin to adenomas of the thyroid gland. Ribbert³ in 1915 resurrected the same belief. One cannot be certain, however, whether he had in mind the "fetal adenoma" exclusively or the comparatively rare true benign neoplasm, or even both types of lesions. While adhering to the fetal origin of the adenoma, he suggested a different mechanism for its formation. He described isolated cell groups in the form of solid epithelial bodies, lying between alveoli that did not possess lumens and were surrounded by a thin layer of connective tissue. Generally not more than two such bodies could be found in a single gland. Ribbert expressed the belief that these were not formed at puberty or when the adenoma first became visible, but that their occurrence must be attributed to rests of embryonal epithelium which did not form alveoli with lumens but continued to form solid cell masses. Thus, while Ribbert's description would indicate that he was considering a true benign neoplasm, his opinions, nevertheless, have become associated with those having to do with the so-called fetal adenoma and the embryonal origin thereof.

Virchow,⁴ Hitzig⁵ and Michaud⁶ represent the school of earlier writers who explained the formation of an adenomatous nodule in the

2. Beck, B.: Ueber eingesackten Drüsengewebe-Kropf, *Arch. f. physiol. Heilk.* **8**:136-138, 1849.

3. Ribbert, H.: Das Adenom der Schilddrüse, *Frankfurt. Ztschr. f. Path.* **18**: 55-56, 1915.

4. Virchow, R.: Die krankhaften Geschwülste, Berlin, A. Hirschwald, 1863, vol. 3, no. 1, pp. 15-17.

5. Hitzig, T.: Beiträge zur Histologie und Histogenese der Struma, *Arch. f. klin. Chir.* **47**:464-502, 1894.

6. Michaud, L.: Die Histogenese der Struma nodosa, *Virchows Arch. f. path. Anat.* **186**:423-477, 1906.

thyroid gland on a basis other than origin from fetal cell rests. Virchow, writing on pathologic tumors in 1863, discussed the process of hypertrophy and of hyperplasia and pointed out that each, at times, is a manifestation of normal growth. By a process of budding in certain parts of the follicles, he explained that small solid cones of cells push themselves into the interstitial tissues and, because of an increase in the latter, become isolated as discrete growths, which eventually acquire a fluid-containing lumen. This process, which he believed to be the fundamental one in the formation of goiter, may be diffuse or focal. He attributed the occurrence of an adenomatous nodule to secondary inflammatory changes.

Hitzig expressed the belief that a nodular goiter begins as a single area of differentiated epithelium, which, by a process of metaplasia, gradually replaces the normal tissue of a lobule or even of a lobe. This process, he explained, is essentially due to a difference in the growth potential of neighboring parts of the gland.

Michaud summarized the beliefs of this group when he said: "We believe as Virchow that a goiter nodule develops out of normal epithelium, with Hitzig's modification that it is simply a substitution of normal thyroid tissue by changed cells which arise from the normal tissue."

In considering the present day concepts of the "fetal adenoma," we find less unanimity of opinion as to its nature than existed among the early writers. On only one point does there seem to be any general agreement, and that is that the lesion is not fetal in origin. While most writers recognize it as an interesting histologic entity, its pathogenesis has not generally been elaborated on. Some positive views have been expressed, which are given here.

Rienhoff and Lewis,⁷ in their discussion of benign tumors, expressed the belief that the term "fetal adenoma" is a misnomer and should be discarded because of insufficient evidence to support the theory of origin from interacinar embryonal cell rests. However, in discussing the hyperplasia-involution cycle, they pointed out that certain glands may undergo an extreme degree of hyperinvolution and that this same type of extreme involutional change is also to be found in the so-called fetal and mixed adenoma.

7. Rienhoff, W. F., and Lewis, Dean: Relation of Hyperthyroidism to Benign Tumors of the Thyroid Gland, *Arch. Surg.* **16**:79-116 (Jan.) 1928. Rienhoff, W. F.: Involutional or Regressive Changes in Thyroid Gland in Exophthalmic Goiter, and Their Relation to Origin of So-Called Adenomas, *ibid.* **13**:391-425 (Sept.) 1926. Lewis, Dean: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1935.

Boyd⁸ stated that many of the nodules which have been regarded as fetal in type are essentially only varieties of the colloid adenoma, since both may be seen shading into the other in the same sections. He noted further three special features about the "fetal adenoma," namely, (1) numerous thin-walled dilated vascular channels, (2) frequent extensive hemorrhages and (3) active budding of the acini within the adenoma. In addition there are a small number of adenomas which have the characteristics of a neoplasm and possibly arise from fetal cells. These are composed of strands of solid clusters of cells with no lumens, supported in a delicate vascular stroma.

MacCallum⁹ rejected the term "fetal adenoma" and considered this lesion as a type of nodular goiter, arising from adult cells and frequently occurring in company with colloid nodules.

Wegelin¹⁰ expressed the belief that the "fetal adenoma" arises in later life from thyroid tissue and is not fetal in origin.

Williamson and Pearse¹¹ stated that the fetal adenoma is a manifestation of a retrogressive phenomenon, attributable to perilobar fibrosis.

Hertzler¹² expressed the belief that the nodule begins as a mass of thyroid tissue which has never reached an adult stage and that it shows malignant tendencies and should be looked on as a true neoplasm.

Kline¹³ cited evidence to support the belief that the development of all forms of adenomatous goiter depends essentially on an irregularity in the degree of proliferation of acini in different portions of the gland.

Else,¹⁴ writing on "Adenomatosis or the Diffuse Adenomatous Goiter," described what he regarded as a clinicopathologic entity characterized by a diffuse new formation of acini, usually involving the entire thyroid gland. In the beginning the growth is of the fetal type without secretion, but later it progresses to the adult type; it does not give rise to symptoms at first, but later signs of hyperthyroidism appear. On studying the pathogenesis of this condition he found masses of

8. Boyd, William: *Surgical Pathology*, ed. 3, Philadelphia, W. B. Saunders Company, 1933.

9. MacCallum, W. G.: *A Textbook of Pathology*, ed. 5, Philadelphia, W. B. Saunders Company, 1932.

10. Wegelin, in Henke, F., and Lubarsch, O.: *Handbuch der speziellen pathologischen Anatomie und Histologie*, Berlin, Julius Springer, 1926, vol. 8, p. 1.

11. Williamson, G. S., and Pearse, I. H.: *The Pathological Classification of Goitre*, *J. Path. & Bact.* **28**:361-387, 1925.

12. Hertzler, A. E.: *Mixed Tumors of Thyroid Gland (Fetal Adenomas)*, *Arch. Surg.* **16**:1187-1200 (June) 1928.

13. Kline, B. S.: *The Origin of Adenomatous Goiter*, *Am. J. Path.* **1**:235-239, 1925.

14. Else, J. E.: *Adenomatosis, or the Diffuse Adenomatous Goiter*, *J. A. M. A.* **85**:1878-1882 (Dec. 12) 1925.

undifferentiated cells, from which arose acini of the fetal type, followed in turn by the formation of a more adult type of colloid-secreting acinus. Different rates of development in various parts of the gland gave the nodular effect, and encapsulation was poor. As to the origin of these new acini, he favored the view that they arise from interstitial cells but also suggested that they may develop from the cells lining the old acini but growing "outside" the walls of these acini. Wilson¹⁵ in 1913 described a similar condition and applied the term "adenomatosis." Goetsch¹⁶ in 1920 described the early stage of this growth, applied the term "diffuse adenomatosis" and regarded the formation of acini as "an abortive attempt at the formation of young small alveoli."

Marine and Lenhart¹⁷ regarded the "fetal adenoma" as a benign tumor which shows wide variations in its histologic picture, particularly in regard to the amount of colloid present and the height of the epithelium. They expressed the belief that it has a period of active growth and a resting period, comparable to physiologic hyperplasia, and, further, that iodine produces no change in the colloid.

HISTOLOGIC DESCRIPTION

The purpose of this paper is to show what we believe to be the origin of "fetal adenoma." This formation is identified by its specific histologic structure, and for clarity we have chosen a typical example for description (figs. 1 to 3).

Under low power magnification, section of such a growth shows a discrete, ovoid nodule, measuring about 4 cm. in its longest diameter and bordered by a thin capsule. This capsule is composed of strands of fibrous connective tissue, enmeshed in which are compressed thyroid follicles lined by atrophic epithelium. A few lymphocytes are present in the interstitial tissue. At irregular intervals the capsule sends fibrous strands into the substance of the nodule for short distances, usually accompanied by blood vessels. The central portion of the nodule is devoid of fibrous tissue.

The supporting framework is a loose reticulum, enmeshed in which is a pale, homogeneous, eosinophilic, acellular matrix. This material resembles intra-acinar colloid in sections stained with hematoxylin and eosin, and it displays the staining reaction of colloid in sections stained by Unna's method.

15. Wilson, L. B.: The Pathology of the Thyroid Gland in Exophthalmic Goiter, *Am. J. M. Sc.* **146**:781-790, 1913.

16. Goetsch, E.: Disorders of the Thyroid Gland, *Endocrinology* **4**:389-402, 1920.

17. Marine, D., and Lenhart, C. H.: The Pathological Anatomy of the Human Thyroid Gland, *Arch. Int. Med.* **7**:506-536 (April) 1911.

The follicles are most abundant at the periphery, and the adjacent capsule is intimately attached. Toward the center of the nodule the follicles become less numerous but otherwise appear to be similar to those at the periphery. The follicles are uniformly small and round and contain little or no colloid; when present, the colloid is pale and vacuolated. The individual cells are uniformly large and high cuboidal and contain abundant cytoplasm, in which granules and vacuoles are seen. The nuclei are large and deeply basophilic, and many show one or more nucleoli. Histologically, these cells appear to be active. In the central, less dense areas, the follicles assume a chainlike configuration, with from three to eight small follicles lying in a row. In some

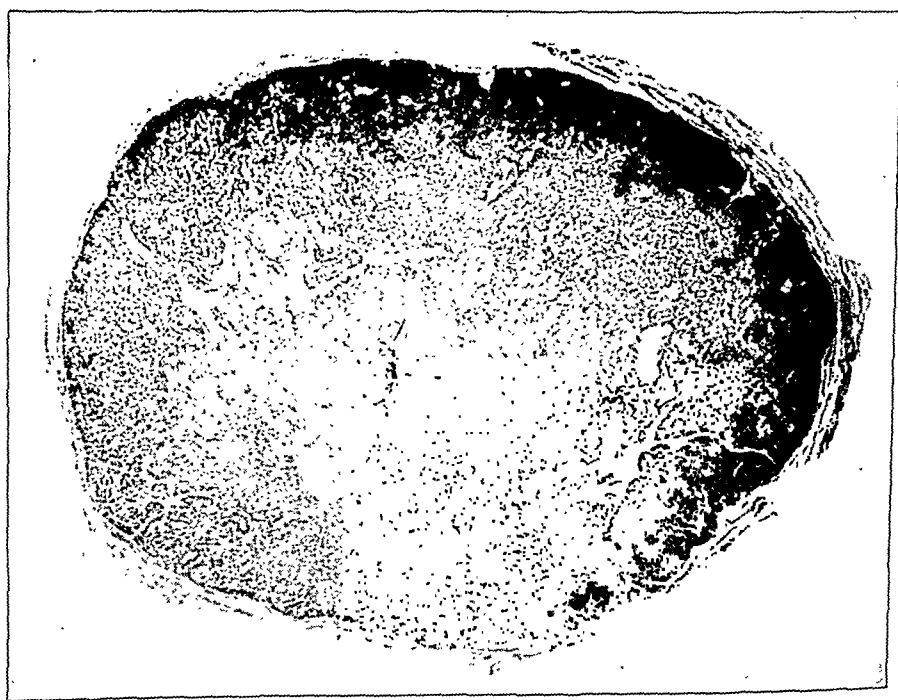


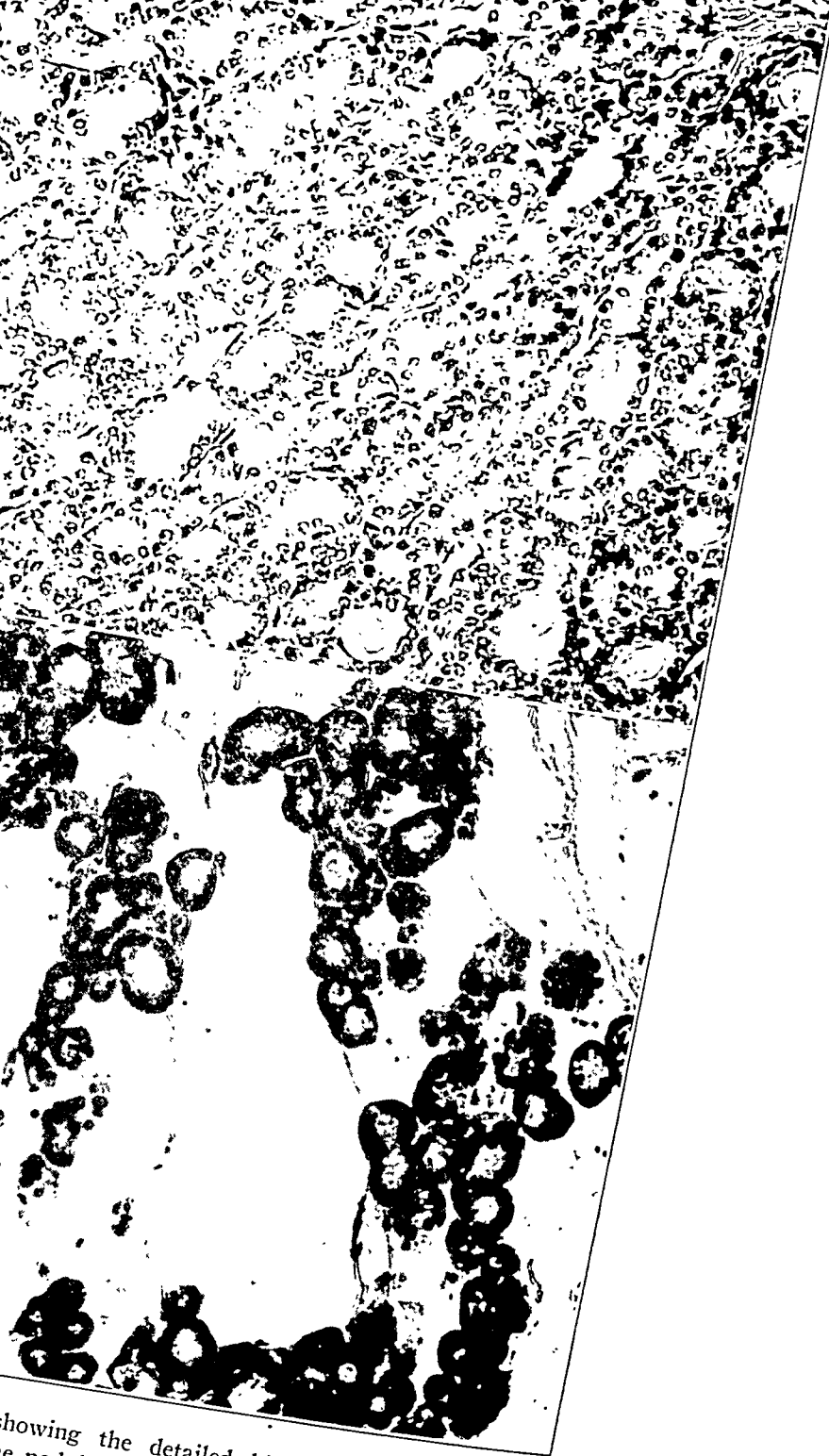
Fig. 1.—Low power photomicrograph of a typical fetal adenoma. Note the capsule and the peripheral concentration of acini.

of these chains a contiguous lumen may be detected. This suggests the formation of new follicles by a process of budding, similar to that which is known to occur in the development of the fetal thyroid. This same chainlike configuration is seen near the periphery, but it is not as apparent there as in the less dense areas.

The nodule is well vascularized throughout. In the capsule, numerous large blood vessels are seen entering the periphery of the nodule. At these points there is a moderate amount of perivascular connective tissue, which appears to be carried in from the capsule. Within the nodule the tissue is even more richly vascularized, the vessels appearing



Fig. 2.—Medium power photomicrographs of the fetal adenoma in figure 1, showing the periphery and the central portion of the nodule. Note the dilated endothelium-bound spaces in the center.



showing the detailed histologic structure at the
e nodule. Note that the epithelium in the center
e periphery.

merely as endothelium-lined spaces lying adjacent to closely packed acini. Near the center these vessels become markedly dilated and possess little or no supporting tissue.

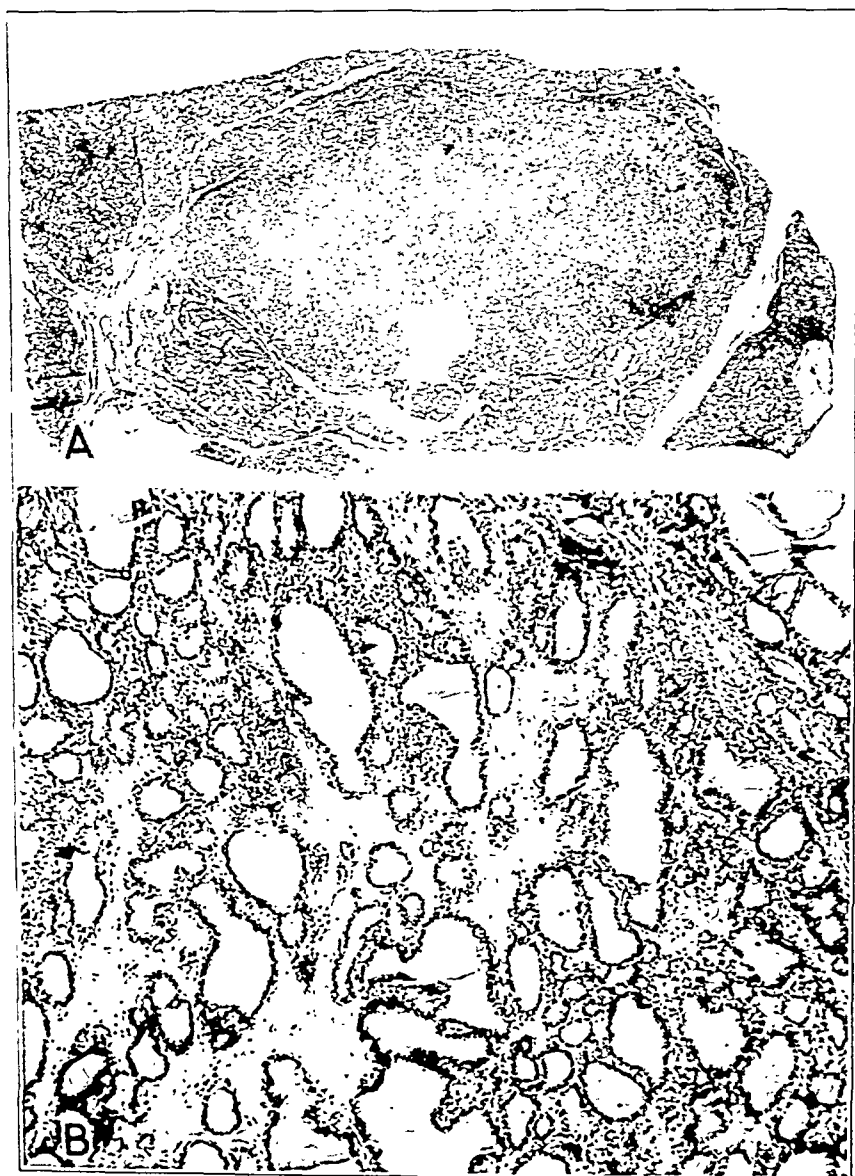


Fig. 4.—*A*, section of a fetal adenoma showing the peripheral acini undergoing hyperplasia and colloid deposition. *B*, high power magnification of the peripheral zone shown in *A*.

Noteworthy features in the foregoing description are (figs. 1 and 3): (1) small acini composed of normal adult thyroid cells; (2) absence of supporting connective tissue; (3) presence of numerous large endothelium-lined spaces, and (4) an acellular colloid-like matrix.

The individual components, acini, blood vessels and interacinar tissue, in this lesion are not characteristic of this particular nodule. It is rather the peculiar pattern they assume which gives the characteristic picture.

We have frequently seen nodules which present the typical appearance of a "fetal adenoma" near the center, while at the periphery they show larger acini composed of normal thyroid cells which are filled

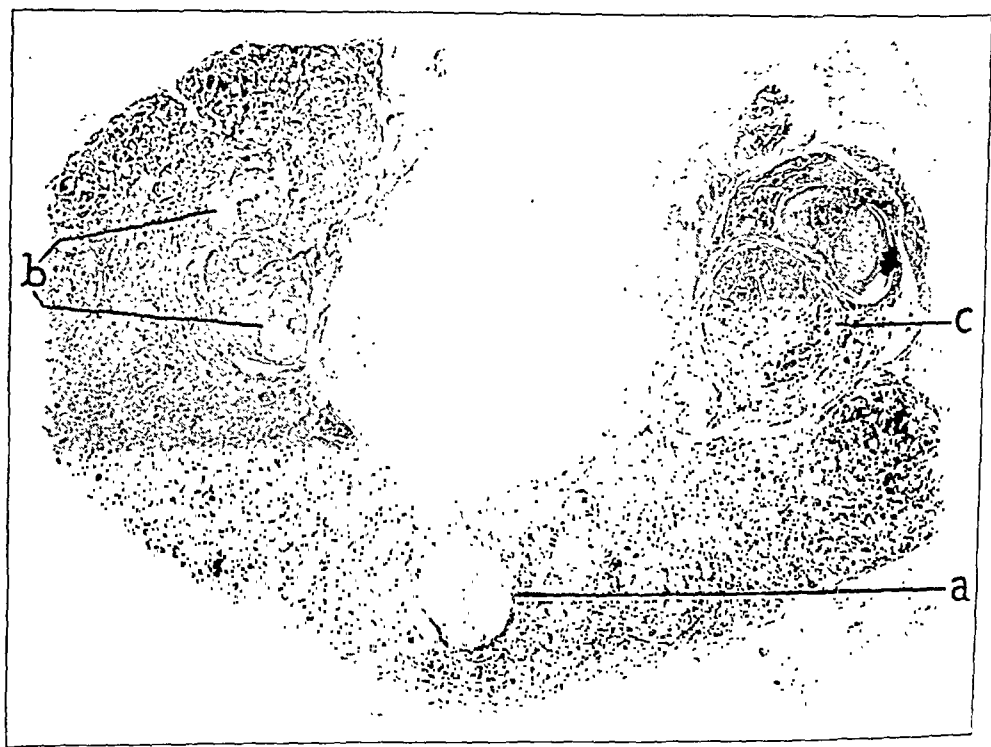


Fig. 5.—A transverse section through the whole gland, showing (a) a colloid body, (b) several colloid bodies into which papilliferous hyperplasia is taking place and (c) a nodule presenting the fetal pattern.

with colloid. In some instances these acini undergo hyperplasia, apparently reacting similarly to the remainder of the gland (fig. 4). On the other hand, we have seen this same picture as focal areas in a non-nodular gland. These changes have been repeatedly observed in routine autopsy material as well as in surgical specimens.

The "fetal adenoma" appears to consist of active thyroid cells, capable of undergoing the same histologic changes as those in a normal gland. We believe that the arrangement of the acini and not the acinus is the typical feature of the "fetal adenoma." This arrangement we

have termed the "fetal pattern." The next step is to show the method of formation of this pattern.

Figure 5 shows a transverse section through both lobes and the isthmus of a thyroid gland removed at autopsy from a 29 year old Negress, who was seven months pregnant, had a 4+ Wassermann reaction and after intravenous injection of thiobismuth collapsed and died in twenty-four hours. There were no apparent signs of hyperthyroidism.

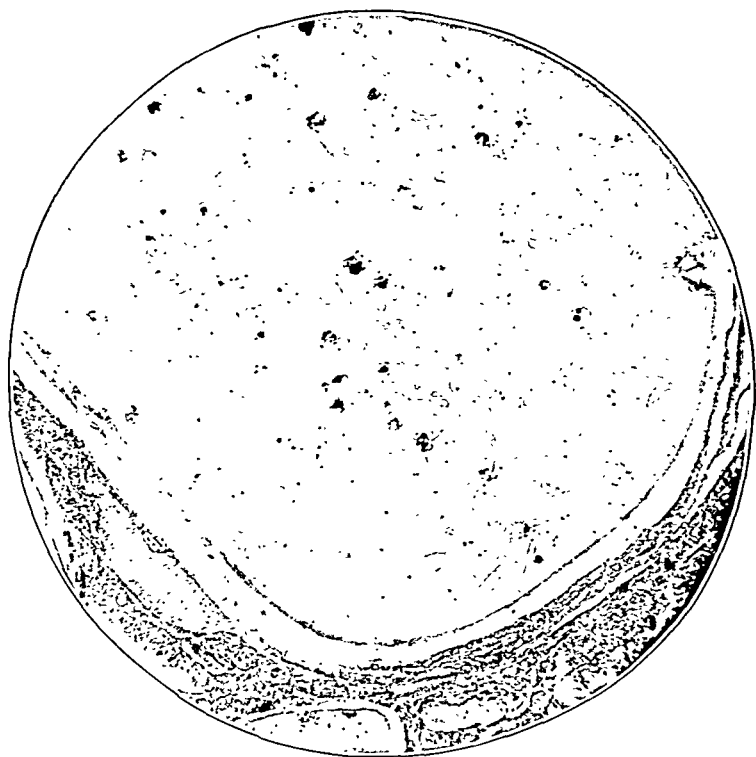


Fig. 6.—High power magnification of the colloid body in figure 5.

On macroscopic examination of the gland on section, about six or eight discrete areas were seen scattered through the gland, giving it a nodular appearance. Microscopically, these areas may be classified in three groups, namely, (*a*) a single large colloid body, (*b*) several colloid bodies within which a papilliferous type of hyperplasia was taking place and (*c*) a large nodule which was almost completely filled by hyperplastic epithelium. The remainder of the gland showed a normal lobular configuration together with manifestations of diffuse hyperplasia.



Fig. 7.—Papilliferous hyperplasia into the colloid bodies shown in figure 5*b*. Note the progressive stages of development as shown in these sections and in those in figure 8.

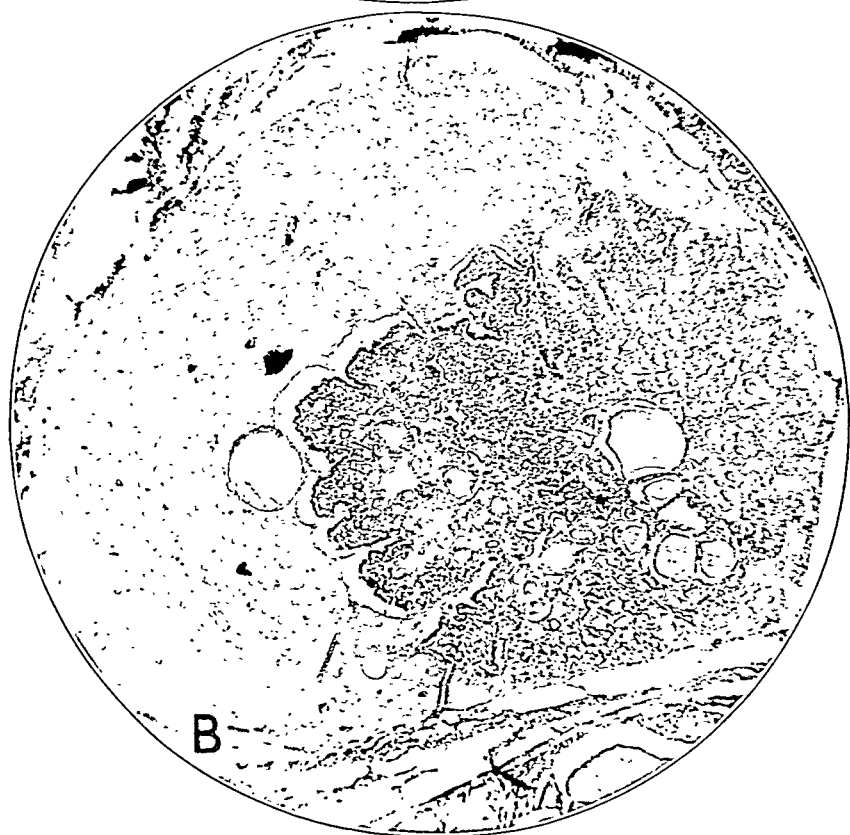
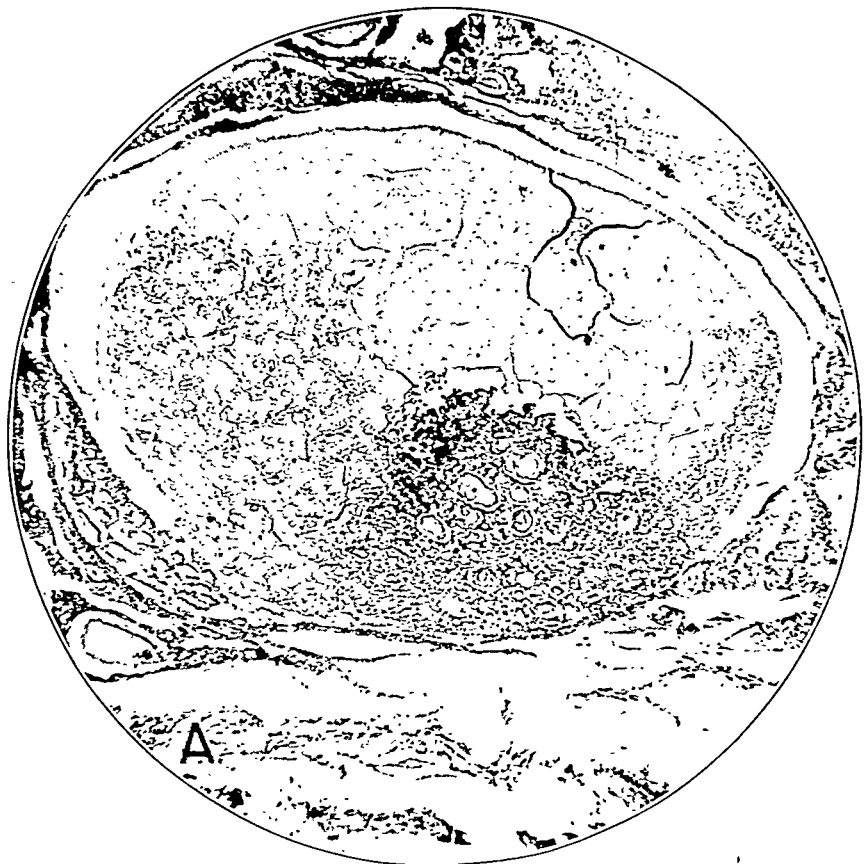


Fig. 8.—Further stages of papilliferous hyperplasia into the colloid bodies.

The single large colloid body (fig. 6), the position of which is shown in figure 5 *a*, was about 0.5 cm. in diameter. It was filled with deep-staining homogeneous colloid. The lining was composed of a single row of flattened epithelium. A pseudocapsule composed of a few loose strands of connective tissue surrounded the follicle.

The colloid bodies in the second group (figs. 7, 8 and 9) varied in size from 0.2 to 0.5 cm. in diameter and were filled with deep-staining, nonvacuolated colloid. One side of the follicle was lined by compressed,

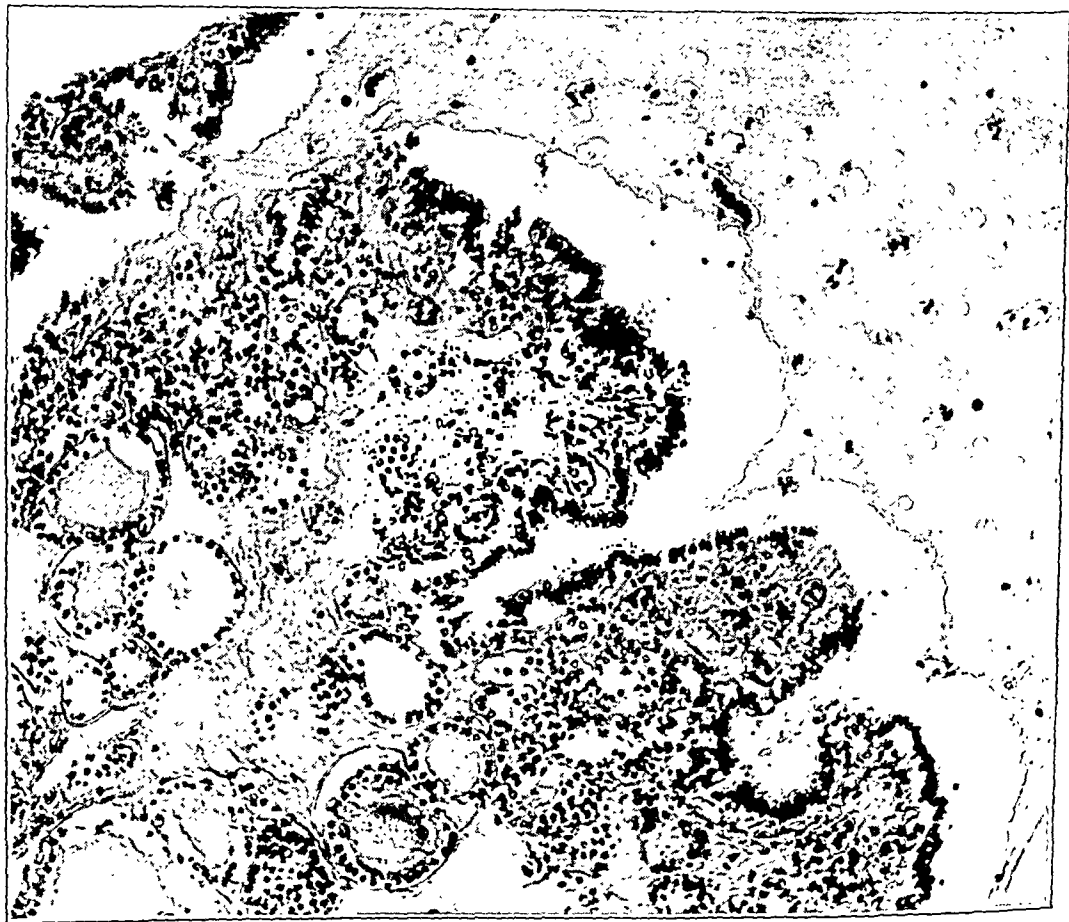


Fig. 9.—High power magnification of the section in figure 8 *B*, showing the typical fetal pattern.

flattened epithelium, while at the opposite side the epithelium was hyperplastic, manifesting itself as a papilliferous type of growth composed of finger-like and clublike projections into the colloid (fig. 9). As this tortuous epithelial wall advanced, it left behind it a matrix of colloid in which were formed numerous small follicles lined with hyperplastic epithelium, which were seen in all stages of development, as they were "pinched" or "budded" by a process of invagination of the epithelial lining. These cells were large and high cuboidal and

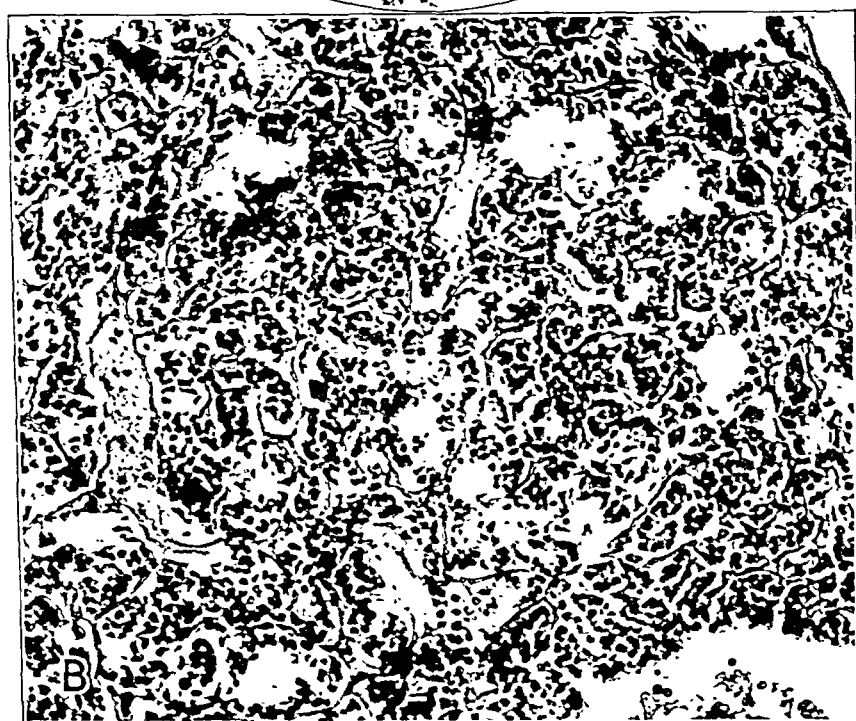
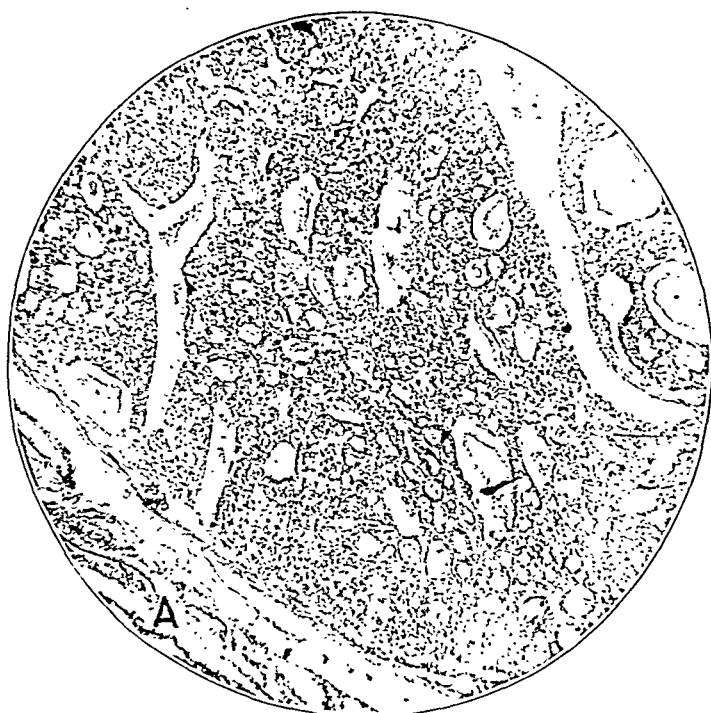


Fig. 10.—*A*, photomicrograph of a solid nodule. Note the similarity to the section in figure 2 *A*. *B*, high power magnification of *A*, showing details of the fetal pattern. Note the similarity of the sections in figures 3 *A* and 10 *B*.

contained abundant pale cytoplasm and large deeply staining granular nuclei. These hyperplastic areas were well vascularized. Numerous engorged vessels lying in close association with the follicles were present. In places, these blood channels might be seen invading the colloid itself. Figures 7 and 8 show the lesion in progressive stages of development in different nodules in the same section.

The large, apparently solid nodule (fig. 5 *c* and fig. 10) was about 1 cm. in diameter. It was surrounded by a narrow zone of loose connective tissue. Its structure was essentially the same as that of the hyperplastic zone found in the colloid bodies just described, the only noteworthy

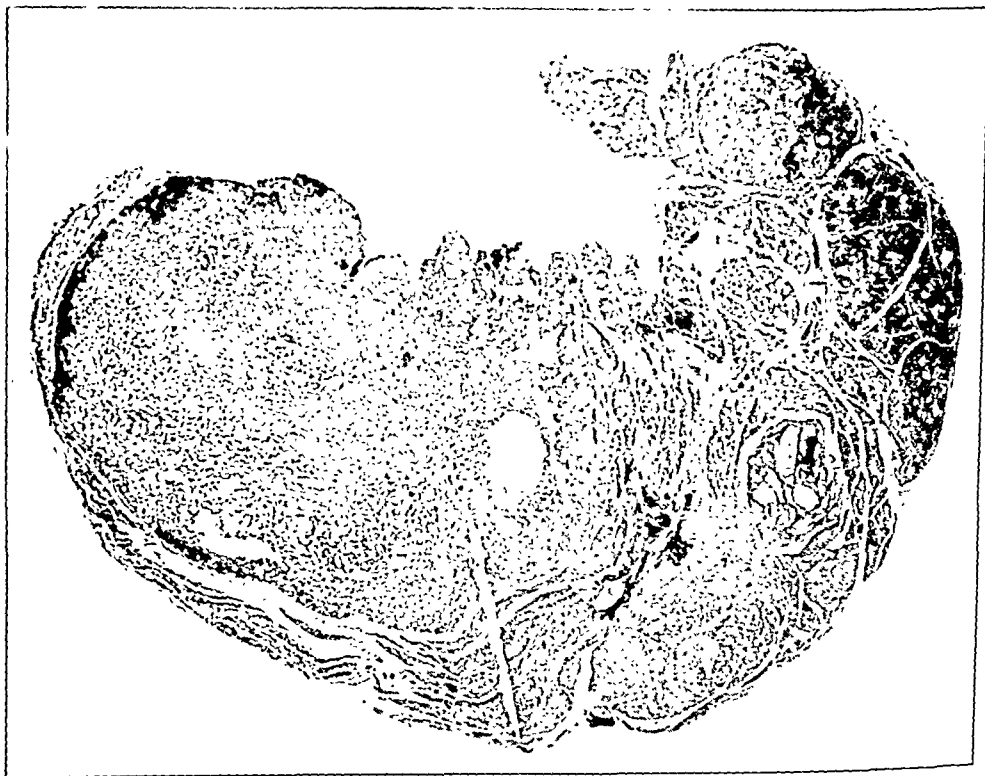


Fig. 11.—A large section through the entire lobe of a thyroid gland, showing a nodule of the fetal type.

difference being that here no colloid was present, the entire nodule consisting of small hyperplastic follicles. The character of the epithelium was identical with that previously described, and the same degree of vascularization was present (fig. 10 *B*). This nodule presented the typical fetal pattern described in figure 3 *A*.

The remainder of the gland showed evidence of hyperplasia of the intravascular type.

We believe that the nodules described were originally colloid bodies. Hyperplasia of the epithelium occurred throughout the gland (a case of pregnancy), and the epithelial lining of the nodules became hyper-



Fig. 12.—Section through the colloid body showing beginning hyperplasia at one border. Figures 12 to 15 are serial sections taken at 100 micron intervals through the same lesion.

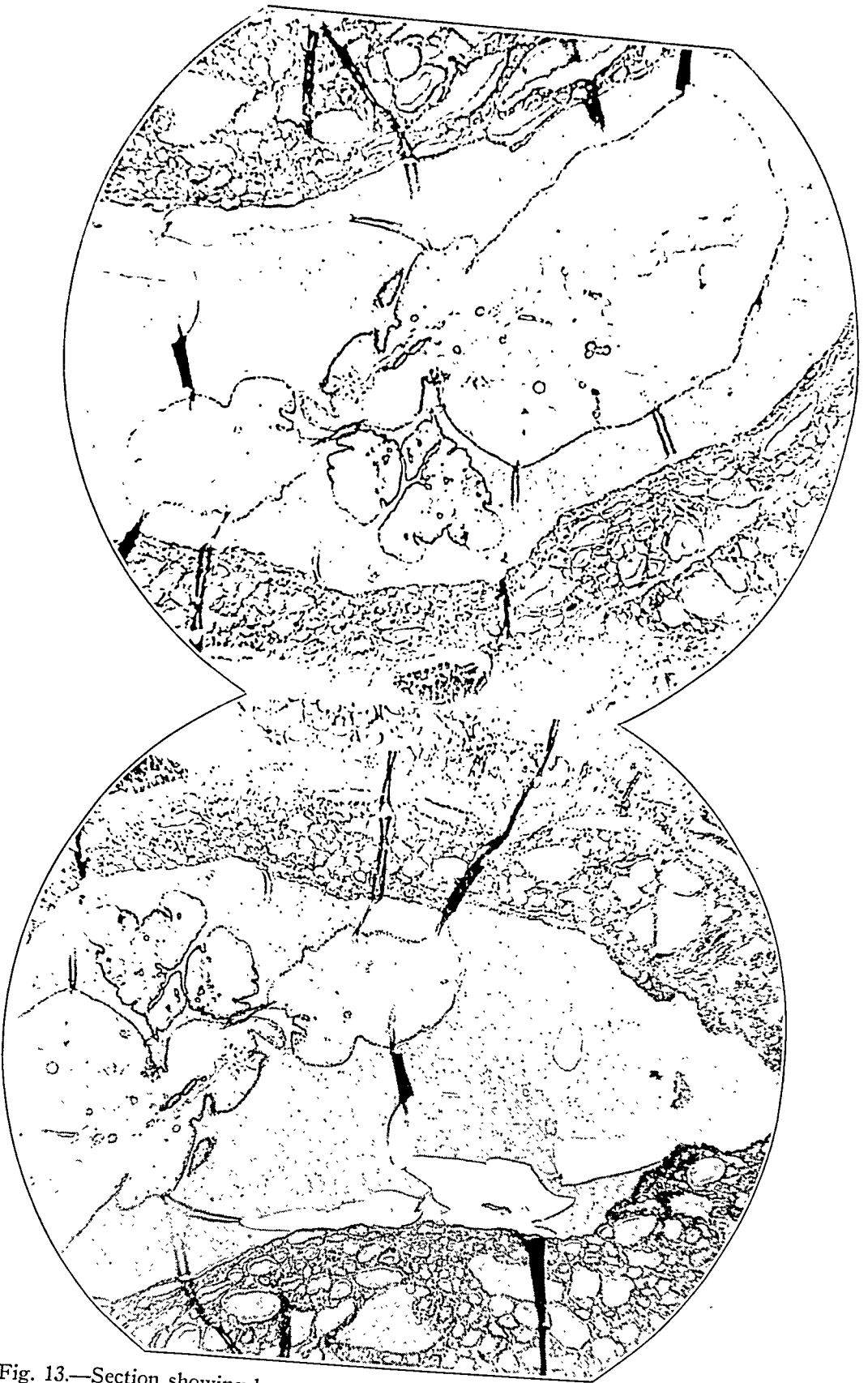


Fig. 13.—Section showing hyperplastic epithelium well advanced into the colloid body.



Fig. 14.—Further stages in the papilliferous ingrowth.

plastic, growing into the colloid. Three stages in the process were evident: (1) an unaltered colloid nodule, (2) the projection of hyperplastic epithelium into the colloid and (3) finally, complete replacement of the colloid by hyperplastic epithelial acini, arranged in the typical fetal pattern. In our routine surgical material this process has been frequently observed both in nodular and in non-nodular glands.

Figure 11 shows a section through the entire lobe of a gland, removed surgically, which to the naked eye presented the features of

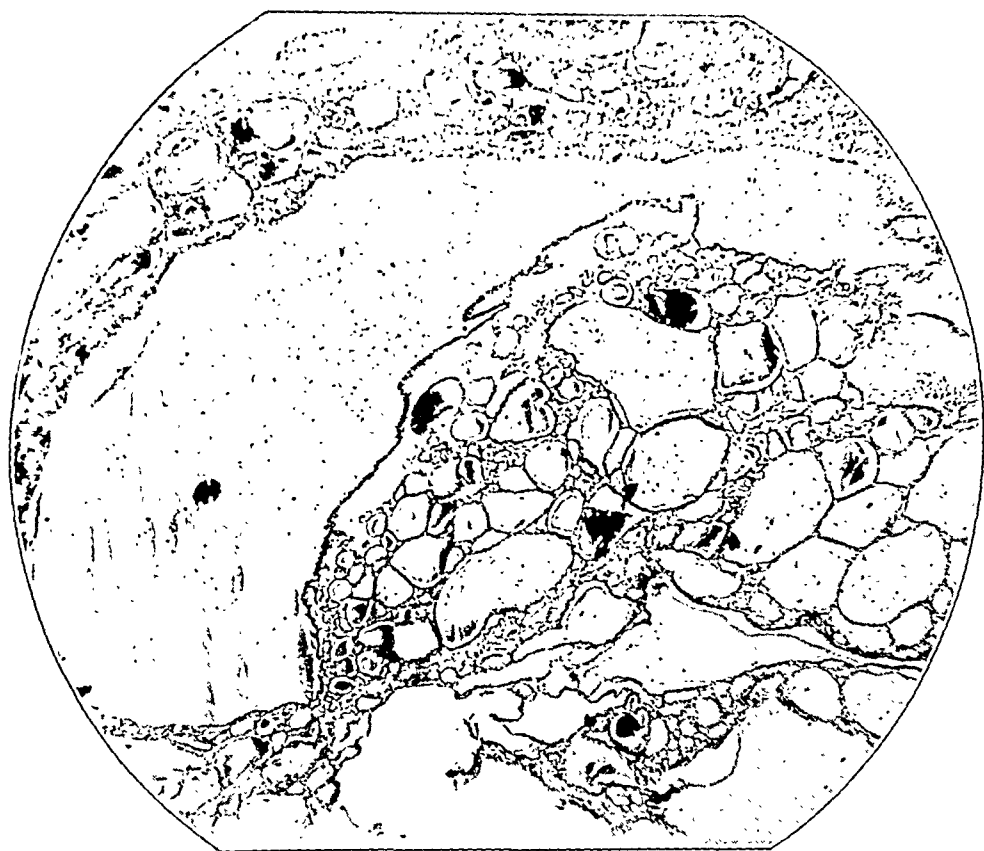


Fig. 15.—Section taken through the colloid body beyond the papilliferous ingrowth.

a nodular goiter containing one large and one small nodule. A large section was made, and the remainder of the gland was cut serially. Section through the larger nodule revealed that it was a fetal adenoma, similar in all essential features to the growth described in figure 1. The small nodule showed a focal area of hyperplastic epithelium, which had undergone moderate involution. The remainder of the gland showed evidence of a residual hyperplasia of a similar type.

Serial sections through non-nodular portions of the gland revealed processes similar to those just described (figs. 12, 13, 14 and 15).

Taking a section at random, for example, that shown in figure 14 *B*, there was to be seen a large irregular colloid body filled with vacuolated colloid. On one side there was a border of flattened epithelium, while on the other side the epithelium was high cuboidal and hyperplastic, causing the outline of the colloid to be irregular, owing to the finger-like and clublike projections which the advancing wall of hyperplastic epithelium sent into the colloid. In the wake of or behind this epithelial wall there was a matrix of pale, eosinophilic, acellular material in which



Fig. 16.—High power magnification of figure 14 *B*, showing marked hyperplasia with new acini in the process of formation.

were found numerous small follicles lined with hypertrophic epithelium and containing deep-staining colloid. Some of these follicles could be seen in the process of formation, as they were "pinched" or "budded" off from the epithelium. This area was well vascularized, numerous small vessels lying in close relationship to the epithelium of the follicles. By serial section the lesion was seen to be a colloid body (fig. 12 *A*) in which a papilliferous type of hyperplasia had occurred (figs. 12 *B* to 16), partially replacing the colloid and reproducing the fetal pattern. Similar areas were noted elsewhere throughout the gland.

In this type of hyperplasia the epithelium carries its blood supply with it, but in this variety of growth apparently the reaction occurs within an epithelium-lined space, and because the colloid gives temporary support to the invading epithelium, no proliferation of fibrous tissue occurs.

The appearance of the nodule depends on the size and on the secondary changes which may occur in it. If the original nodule is small, complete replacement by closely packed acini occurs (fig. 10 *A*), whereas in the larger lesions the replacement is incomplete, the acini

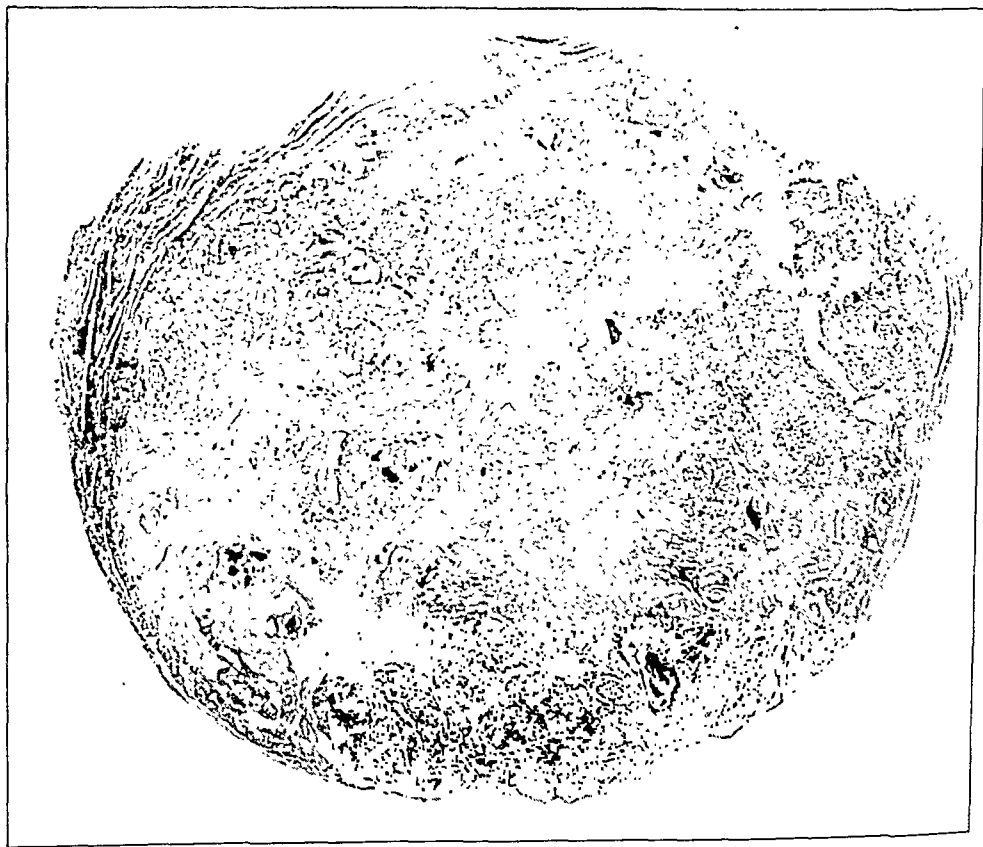


Fig. 17.—Low power magnification of a fetal nodule, showing marked secondary changes of hemorrhage cyst formation and scarring.

being aggregated near the periphery close to the parent epithelium and widely scattered toward the center (fig. 1). As the colloid which originally supported the acini and blood vessels disappears, the capillaries dilate and rupture with resultant hemorrhage. Once hemorrhage has occurred, the initial picture is altered, and secondary changes, such as necrosis, cyst formation, scarring, hyalinization and calcification, may ensue, serving to alter or completely destroy the appearance of the initial nodule.

In the material examined, we were unable to trace any relationship between growth and carcinoma. However, in going over our material, Dr. Douglas Symmers suggested that the mode of origin herein demonstrated tends to support the belief that this type of lesion is sometimes prone to develop carcinoma because, although the new hyperplastic acini may become normally functioning thyroid epithelium, the abnormal method of their development may become still further diverted.

CONCLUSIONS

1. The nodule known as "fetal adenoma" is composed of regenerating thyroid epithelium, occurring in a colloid follicle or body.

2. This follicle may be small or large and encapsulated or non-encapsulated.

3. The peculiar appearance is due to the fact that the proliferation of epithelium occurs into the colloid, which supports the growth, eliminating the immediate necessity of fibrous supporting tissue.

4. In the larger nodules, as the colloid disappears the acini are left without apparent supporting tissue, except for the capillaries, which may become markedly dilated, thus giving rise to the peculiar appearance of the central portion of these growths.

5. Once the lesion is fully formed, there are four possibilities:

(a) The acini may function as normal thyroid epithelium.

(b) They may undergo hyperplasia, forming the nodular hyperplastic goiter, or so-called toxic adenoma.

(c) They may become carcinomatous.

(d) Hemorrhage may occur into the nodule followed by secondary degenerative changes, such as necrosis, cyst formation and fibrosis.

EXPERIMENTAL JOINT SPRAIN

PATHOLOGIC STUDY

LEO J. MILTNER, M.D.

C. H. HU, M.D.

AND

H. C. FANG, M.D.

PEIPING, CHINA

In a previous communication¹ the pathologic changes which followed the production of mild sprain in the knee joint of the rabbit were reported. Since that time, other similar experiments have been performed which are of greater interest, particularly since the results suggest the pathologic basis for the clinical condition termed chronic traumatic arthritis. As a foundation for the discussion, a résumé of the results in the most recent group of experiments together with those reported² previously is given.

METHOD

After varying amounts of manual force were applied to the knee and ankle joints of ten rabbits, a method was developed for the production of mild and severe forms of sprain without roentgenographic evidence of fracture.

In this manner, mild sprains were produced in twelve rabbits (group 1) and severe sprains in eleven (group 2). Roentgenograms of all sprained joints were taken immediately thereafter, and no evidence of injury to the bone was demonstrated. Autopsy was performed on the animals in group 1 in from one to six weeks after production of the sprain and on those in group 2 in from one to eleven weeks later. The joints were removed, roentgenograms were again taken and the specimens were examined grossly and microscopically.

Mild and severe sprains were produced in the same manner in a third group of twelve rabbits, and the sprained knee joints were immobilized in plaster of paris casts. Attempts were made to determine the effects of immobilization on the rate of healing, but since it was difficult to maintain satisfactory immobilization, the results were discarded.

RESULTS

Pathologic Changes After Mild Sprain (Group 1).—One week after mild sprain there was definite swelling of the joints. The synovial

From the Division of Orthopedic Surgery, Department of Surgery and the Department of Pathology, Peiping Union Medical College.

1. Miltner, Leo J., and Hu, C. H.: Experimental Reproduction of Joint Sprain, *Proc. Soc. Exper. Biol. & Med.* **30**:883, 1933.

2. Miltner, Leo J.; Hu, C. H., and Fang, H. C.: The Pathology and Treatment of Joint Sprain, *Chinese M. J.* **49**:521, 1935. Miltner and Hu.¹

membrane was edematous and had small foci of hemorrhage (fig. 1) and a few dilated blood vessels near its surface. The joint fluid was increased in amount and was more viscous and yellower than normal. There was slight pannus formation at the osteocartilaginous junctions on the injured side. The subcutaneous tissue and the loose connective tissue of the mesotendons showed evidence of hemorrhage. There was no blood within any of the tendon sheaths. Microscopic sections showed hemorrhage into and under the synovial membrane. The synovial cells showed marked vacuolation. The subsynovial tissue was edematous, with capillary congestion, early fibroblastic proliferation and considerable infiltration with leukocytes and lymphoid cells. In places the surface of the synovial membrane was covered with fibrin, while in

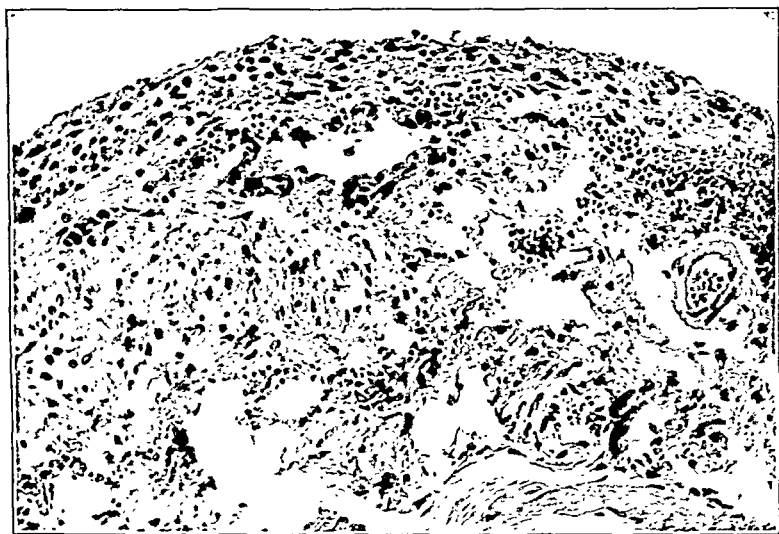


Fig. 1.—Photomicrograph ($\times 200$) of the synovial membrane of a joint one week after mild sprain. Note the edema and foci of hemorrhage and early proliferation of fibroblasts in the loose subsynovial connective tissue. Other sections in the same area show infiltration with leukocytes and lymphoid cells.

others the fibrin was seen in the subsynovial tissues. Near the attachments to the bone, the injured capsule and ligaments showed similar changes consisting of edema, fibroblastic proliferation and infiltration with lymphoid cells. The loose connective tissue beneath the synovial lining of the tendon sheaths presented a picture essentially the same as that seen in the synovia.

Two and three weeks after the sprain there were still definite signs of acute inflammation of the synovial tissue. There was a great increase in the number of fibroblasts in the subsynovial tissue. Hemosiderin was found in large amounts in the phagocytic cells of the inflamed area.

At this stage hyalinized masses of fibrin were seen within the synovial tissue and on the synovial surface (fig. 2). The tendon sheaths and the soft tissue surrounding the capsule and ligaments showed changes similar to those which were found after one week, except that there was more marked fibroblastic proliferation.

After four weeks, there was no external evidence of swelling or other signs of old injury. Microscopic examination of the tendon sheaths, synovial tissue and ligaments still showed evidence of old hemorrhage. The number of fibroblasts was decreased, but the number of collagen fibers was increased. Many small capillaries were seen in this young connective tissue. In certain places the synovial membrane showed small foci of necrosis, with deposits of fibrin on the surface. There

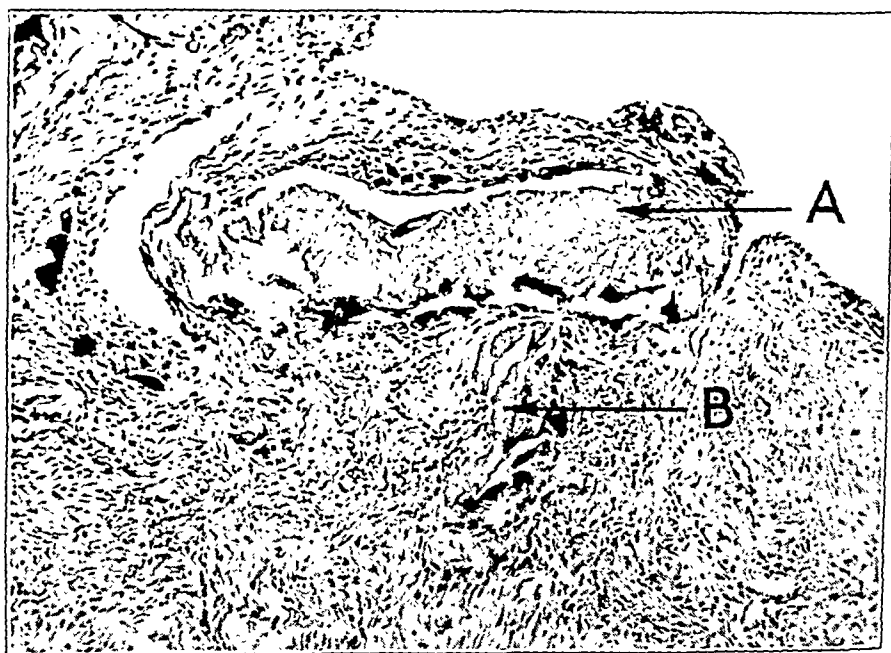


Fig. 2.—Photomicrograph ($\times 180$) of the synovial membrane of a joint three weeks after mild sprain. Note the hyalinized mass of fibrin (A) between the villi and (B) within the subsynovial connective tissue.

was still an appreciable amount of edema of the loose connective tissue, but the infiltration with leukocytes and lymphoid cells was much less than that shown in the sections taken after three weeks.

Microscopic examination at six weeks showed complete healing of the traumatized parts. There was a late stage of fibrosis, with shrinkage and contraction of the connective tissue structures.

Pathologic Changes After Severe Sprain (Group 2).—In addition to the changes just described (after mild sprain), the joints subjected to severe sprain showed the following pathologic changes: A fibrillar degeneration of the surface layers of the cartilage was seen, especially

at the margins of the joint surfaces on the affected side. New fibroblasts, apparently arising from the synovial membrane, had already attached themselves over these areas of cartilage as early as the second week. The inner free portion of the semilunar (fibrous) cartilage on the affected side showed slight necrotic changes. After six weeks, the distal free ends of the semilunar cartilage showed a more advanced stage



Fig. 3.—Photomicrograph ($\times 234$) of the hyaline cartilage on the side of the joint (side of compression) opposite to the sprained ligaments, ten weeks after severe sprain. Note that many of the cartilage cells of the intermediate area (I) show only faint staining, while others have degenerated completely.

of the fibrillation with exfoliation of the superficial layers and hyalinization of the deeper layers of cells. At the end of the eighth and tenth weeks, several specimens showed complete degeneration of the free portion of the semilunar cartilage. In all the specimens the intra-articular cartilage of the tibia on the side of the joint opposite to the

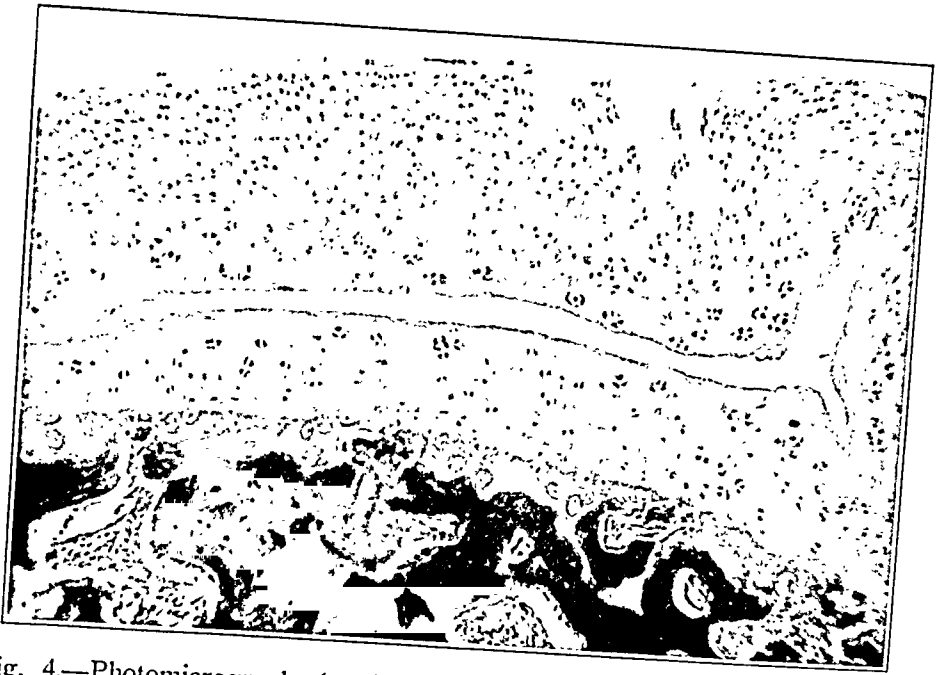


Fig. 4.—Photomicrograph ($\times 70$) of the hyaline cartilage ten weeks after severe sprain. Note the horizontal fissure caused by trauma. Numerous necrotic cartilage cells may be seen at the margins of the fissure.

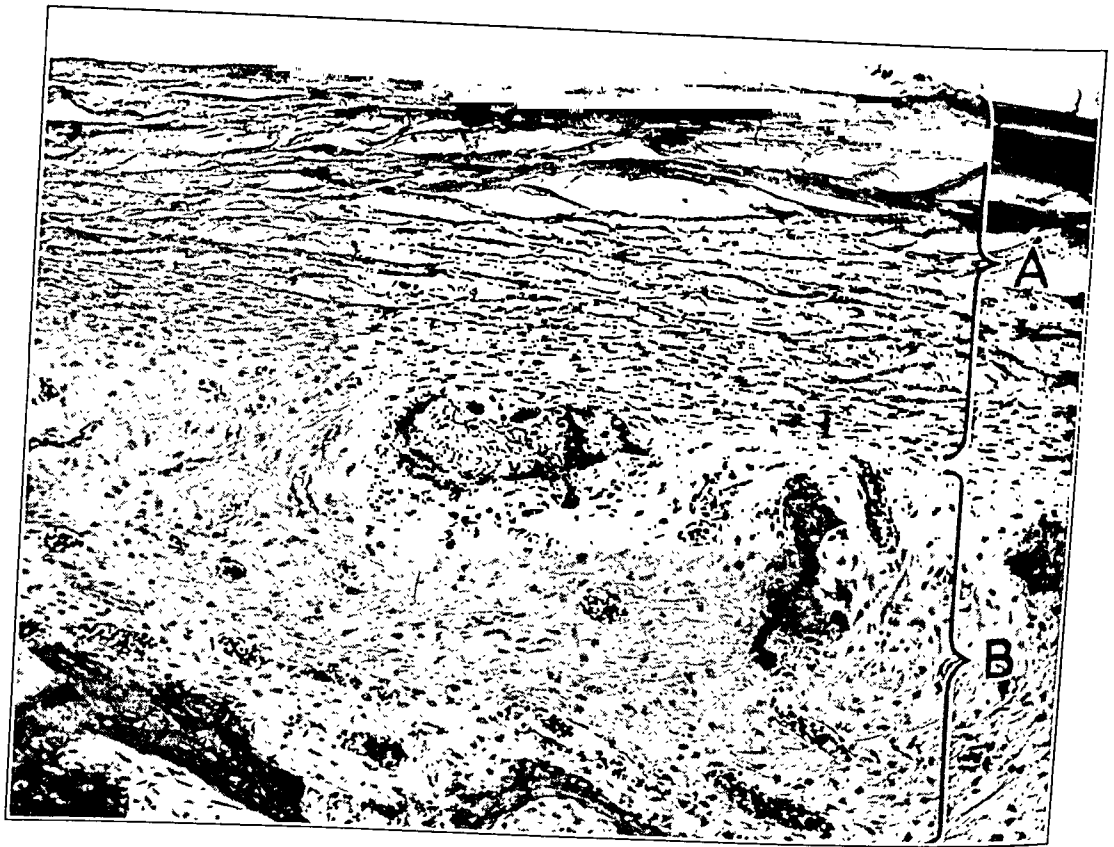


Fig. 5.—Photomicrograph ($\times 113$) of the point of insertion of ligament into bone eight weeks after severe sprain. Note (A) the ligament and (B) the typical area of vascular callus with detached bits of bone which failed to cast a shadow in roentgenograms.

sprained ligaments showed numerous scattered cartilage cells, which were faintly or heavily eosinophilic in contrast to the normal cartilage cells which had taken up a deep basic stain. These eosinophilic cartilage cells showed other definite evidence of degeneration, such as fragmentation of the nuclei and shrinking of the cytoplasm (fig. 3). A horizontal fissure within the substance of the articular cartilage was found in one knee joint (fig. 4). In most of these specimens microscopic examination showed definite evidence of a tearing injury at the point of insertion of ligaments into the bone. Small bits of bone had been torn loose and tended to grow in the new location (fig. 5). At these points of insertion of ligaments there was a large increase of the fibroblasts with vascular dilatation and infiltration with round cells. Here, the process of repair persisted for as long as from eight to ten weeks. The synovial membrane showed a persistence of the previously described inflammatory changes for as long as from six to eight weeks.

COMMENT

These experiments demonstrate that trauma applied to joints causes an acute inflammatory reaction at the points of greatest injury. If the injury is severe enough, the bony or cartilaginous structures may be involved. These structures heal slowly under ordinary circumstances; therefore, the inflammation may become chronic. In the mild form of sprain there is an immediate response of the most vascular structures. The early increase in the activity of the synovial membrane with the exudation of synovial fluid is a condition which is known clinically as traumatic synovitis. At the same time there is edema of the loose subsynovial tissues and of the loose periarticular connective tissues, especially those near the tendon sheaths on the affected side of the joint. In the joints of the rabbits in group 1 (those with mild sprain) the external signs and gross evidence of pathologic change disappeared by the fourth week, but the microscopic evidence of inflammation (slight edema and fibrosis of the connective tissues) persisted until the end of the sixth week. This change is of clinical interest, since it suggests that the joint should be protected or supported for at least two weeks after the clinical signs have disappeared.

In the joints of the rabbits in group 2 (those with severe sprain without roentgenographic evidence of fracture) the inflammatory reaction of the soft tissues was similar in nature but more severe in degree than that found in the joints of the rabbits in group 1. The microscopic changes of the soft tissues usually persisted until the sixth to the eighth week and resolved gradually during the eighth to the tenth week. In addition to the microscopic changes found in the joints of the rabbits in group 1, there were evidences of injury at the point of insertion of

ligaments into the bone and of the joint cartilage. At the ligamentous-ossseous junctions detached bits of bone were usually seen. These bits of bone were microscopic in size and failed to throw a shadow in the roentgenograms.

Of greater interest were the changes in the intra-articular hyaline cartilage of the tibia on the side of the joint opposite to the sprained ligaments. Since the normal cartilage covering the surface of the tibia is approximately twice as thick as that which covers the convex surface of the corresponding condyle of the femur, it is believed that its intermediate or less compact area is more subject to a compression type of injury. The uniform finding of degeneration of the cells in the intermediate zone of the cartilage bears out this contention. It is further believed that this slow degeneration of the cartilage may produce not only local but remote effects on the more vascular structures of the joint and that therein lies one of the causes for the condition termed chronic traumatic arthritis. The traumatic fissure in this intermediate zone of the cartilage, although found in only one case, also adds evidence to show that this tissue is vulnerable to ordinary trauma.

SUBPHRENIC ABSCESS

AN ORIGINAL EXTRAPLEURAL OPERATION

GOLDER L. McWHORTER, M.D.

Clinical Associate Professor of Surgery, Rush Medical College of the
University of Chicago
CHICAGO

A subphrenic abscess may be defined as one which at some point is in contact with the under-surface of the diaphragm. Barlow described the condition in 1845, while Volkmann recorded the first operation in 1879.

It is my purpose to emphasize the importance of early diagnosis and operation, to report my cases and also an original, safer, transcostal, extrapleural method of drainage and to point out the necessity for choosing the most suitable operative route, depending on the location and the size of the abscess.

The subphrenic area is considered to be that space bounded above by the diaphragm and below by the transverse mesocolon. This space may be divided for clinical purposes into a suprahepatic and an infrahepatic space, and these may be divided into lesser but less completely separated spaces. A subphrenic abscess may occupy all or only a part of one or more adjoining spaces, depending on limiting adhesions.

The subphrenic space is divided as follows:

1. The suprahepatic space

- Right intraperitoneal anterior superior space
- Right intraperitoneal posterior superior space
- Right extraperitoneal superior space, between the layers of the coronary ligament
- Left intraperitoneal anterior superior space

2. The infrahepatic space

- Right intraperitoneal inferior space
- Left intraperitoneal inferior anterior space
- Left intraperitoneal inferior posterior space (bursa omentalis)
- Left extraperitoneal inferior retrosplenic space (Barnard¹)

A subphrenic abscess originates from a perforated peptic ulcer in about one third of the cases and from a suppurative appendicitis in

Read before the Western Surgical Association, Dec. 12, 1935.

1. Barnard, H. L.: Surgical Aspects of Subphrenic Abscess, Brit. M. J. 1:371, 1908.

a third. It occurs frequently by direct extension from the appendix along the outer gutter of the ascending colon into Morison's pouch. Occasionally it may follow an infection or an injury to the liver, gall-bladder, pancreas, colon, spleen or kidney or to other abdominal structures (Harper and Thomas²).

Rarely it may result from a metastatic infection, from extension of an infection from above the diaphragm or from osteomyelitis of a vertebra (Barnard).

The importance of the lymphatics in carrying infection from the colon and especially from the ileocecal region has been emphasized by Truesdale.³

Some abscesses which occur in the right posterior extraperitoneal space after a subsiding appendicitis, as in case 6, undoubtedly arise from infection along the lymphatics.

Subphrenic abscess occurs about three times more frequently in males than in females (Ochsner and Graves⁴). This may be due to the greater frequency of perforated peptic ulcer and of appendicitis in the male. Ochsner and Graves found that 70 per cent of the abscesses they observed occurred in persons from 9 to 40 years of age. They observed that only about 30 per cent of subphrenic infections went on to supuration, the remainder subsiding spontaneously.

Anatomically, the superior surface of the liver, like the right surface and the most of the anterior surface, lies directly against the diaphragm and is curved corresponding to the dome of that structure. The superior surface reaches higher up on the right than on the left, while the center is slightly depressed. The junction of the superior and the posterior surfaces forms a rather blunt margin. The uneven posterior surface is shaped somewhat like a rectangular triangle. It is curved so as to be convex on the right side. From right to left may be found the fossa venae cavae, the impression for the adrenal gland, the lobus caudatus, the fossa ductus venosi and the impression for the abdominal esophagus. The liver is covered for the most part by the tunica serosa. There are four or five small areas and one fairly large one on the posterior surface of the right lobe which lie extraperitoneally.

Anteriorly, the ligamentum falciforme hepatis passes from the abdominal wall and the diaphragm near the midline to the superior

2. Harper, F. R., and Thomas, C. A.: Subphrenic Abscess Following Trauma, *J. A. M. A.* **105**:1267 (Oct. 19) 1935.

3. Truesdale, P. E.: Origin and Course of Infection in Subphrenic Abscess, *Ann. Surg.* **98**:846 (Nov.) 1933.

4. Ochsner, A., and Graves, A. M.: Subphrenic Abscess: Analysis of 3,372 Collected and Personal Cases, *Ann. Surg.* **98**:961 (Dec.) 1933.

surface of the liver. At the cardiac impression of the liver the two layers forming the peritoneal fold diverge from one another and go over into the anterior lateral layers of the ligamentum coronarium hepatis from the inferior surface of the diaphragm approximately in a frontal plane to the upper surface of the liver. The peritoneum forming the posterior layers of the coronary ligament comes from the posterior surface of the diaphragm or from the anterior surface of the right kidney, the adrenal gland or the flexura coli dextra and is sometimes called the ligamentum hepatorenale (Spalteholz⁵ and Cunningham⁶).

On the left the anterior and posterior layers of this ligament come together quickly and form the ligamentum triangulare sinistrum hepatis. At the right of the fossa venae cavae the anterior and posterior layers of peritoneum are widely separated, leaving a large uncovered area on the posterior surface of the liver, which is limited at the right by their junction into the ligamentum triangulare dextrum hepatis.

There is considerable normal variation in the level of reflection of the pleura at the costophrenic angles, forming a variable width of extrapleural diaphragm through which transcostal drainage of a subphrenic abscess might be established. Corning⁷ pointed out that the height of the diaphragm varies at different ages. In the new-born infant it may be found at the level of the fourth rib on the right side. In a 36 year old man the diaphragm may be midway between the fifth and the sixth rib, while in a 72 year old man it may be below the sixth rib (fig. 1). In the presence of emphysema one will find the diaphragm lower than usual, and when there are old pleural adhesions it may be somewhat fixed, increasing the difficulties of diagnosis.

SYMPTOMS AND DIAGNOSIS

The symptoms of a subphrenic abscess vary to a large extent, depending on the source, location and size of the abscess. Elsberg⁸ pointed out that they may develop days, weeks or months after an attack of appendicitis or an operation. Usually there is a history of a recent acute attack of appendicitis, cholecystitis, a perforated peptic ulcer or an operation. The temperature may persist or drop temporarily and then

5. Spalteholz, W.: *Atlas of Human Anatomy*, ed. 3, translated by L. F. Barker, Philadelphia, J. B. Lippincott Company, 1910.

6. Cunningham, J. D.: *Text-Book of Anatomy*, ed. 6, New York, William Wood & Company, 1931.

7. Corning, H. K.: *Lehrbuch der topographischen Anatomie für Studierende und Aerzte*, ed. 3, Wiesbaden, J. F. Bergmann, 1911, p. 283.

8. Elsberg, C. A.: *A Contribution to the Pathology, Diagnosis, and Treatment of Subphrenic Abscesses After Appendicitis*, *Ann. Surg.* **34**:729, 1901.

increase steplike each day, with an increase of systemic toxemia together with local symptoms of suppuration.

The peritoneum over the diaphragm is supplied from the phrenic nerve; consequently inflammation may cause referred pain in the shoulder and neck, where it is supplied by cutaneous nerves from the fourth

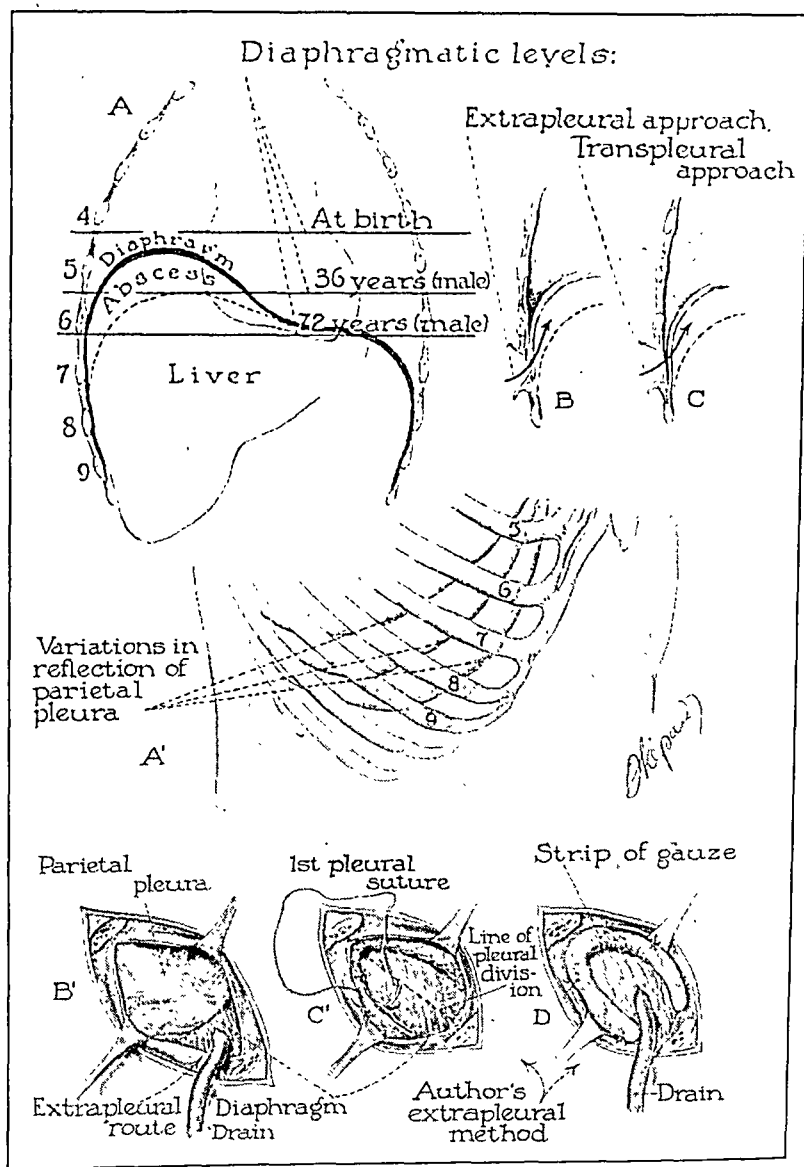


Fig. 1.—A and A' show normal variations in the height of the diaphragm and its pleural reflections. In B and B' is shown the transcostal extrapleural method of drainage, which may be used with a high pleural reflection; in C, the transcostal route which is frequently used to open the pleural cavity in the absence of adhesions; in C' and D, my method. In the last method, after resection of one rib in the axillary line, the costal and diaphragmatic pleural layers are incised, and the edges are dissected laterally and sutured, forming an extrapleural area on the diaphragm for drainage.

cervical segment (Christopher⁹). The lateral and anterior portions of the abdominal peritoneum are supplied by the lower intercostal and first lumbar nerves, and the central posterior and the pelvic portions of the peritoneum, chiefly by the sympathetic system (Cope¹⁰).

At the onset there may be limited or painful respirations owing to immobilization of the diaphragm or to a pleuritis, which is more marked in the case of a suprahepatic abscess and less noticeable when the abscess is located below the reflection of the pleura. Later there is practically always limitation of movement of the diaphragm, but the amount of elevation is variable, depending on the size and location of the abscess.

A fluoroscopic examination or roentgenograms taken from several angles and with the patient upright may fail to demonstrate a small

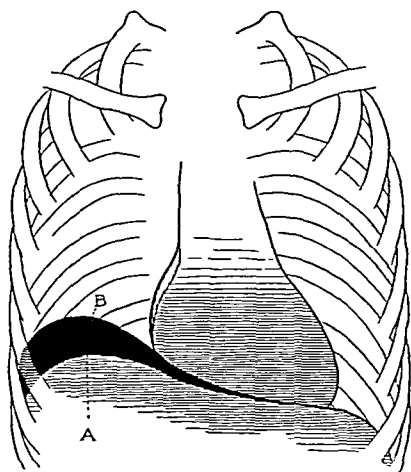


Fig. 2 (case 3).—Drawing made from roentgenograms which at the onset of symptoms showed only slight elevation of the diaphragm (*A*), but one week later (*B*) there were marked elevation of the diaphragm and also distortion of the heart due to an abscess of the superior anterior space which contained no gas.

suprahepatic abscess. When the abscess is large there may be extension forward and downward, with a visible swelling and an area of dulness over the abdomen forming a triangle bounded by the falciform ligament, the transverse colon and the right costal border.

In cases in which the diagnosis is doubtful examinations should be repeated in a few days, and a comparison made of the level and immobility of the diaphragm (fig. 2 *A-B*). In a few cases gas and a shifting

9. Christopher, Frederick: Neck Pain in Subphrenic Abscess, *Ann. Surg.* 85:318, 1927.

10. Cope, V. Zachary, in Walton, A. J.: *A Text-Book of Surgical Diagnosis*, New York, William Wood & Company, 1928, chap. 2, p. 697.

fluid level can be demonstrated both by roentgenographic and by physical examination (fig. 3).

The early friction sounds and symptoms of pleuritis over the costophrenic region may disappear with effusion in the pleural cavity. It is often difficult to establish a differential diagnosis between abscess and bronchitis, pulmonary inflammation, pleuritis or atelectasis. The diagnosis was correct in only 38 per cent of the 18 cases reported by Brown.¹¹ Fever and the degree of toxemia, as indicated by a marked leukocytosis, vary with the acuteness and activity of the abscess but are increased out of proportion to the pulmonary findings.

An abscess involving the suprahepatic posterior intraperitoneal space may differ roentgenographically from one involving the anterior space in that in the anteroposterior view of the former the costophrenic

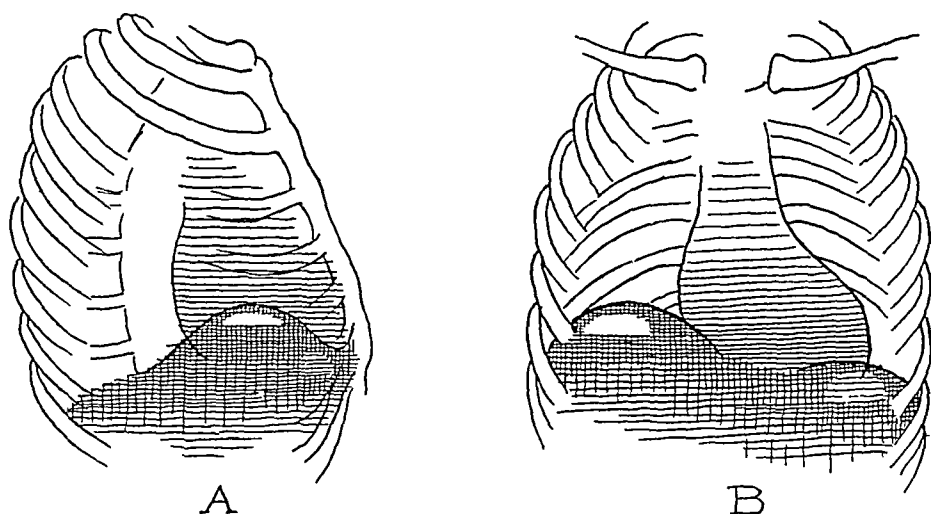


Fig. 3 (case 4).—Elevation of the diaphragm due to an abscess containing gas. There was slight increased density in the lower lobe of the lung. Transcostal extrapleural drainage was done (fig. 1, C' and D).

instead of the cardiophrenic angle is obliterated and in the lateral view the posterior instead of the anterior costophrenic angle is obliterated.

When the abscess involves the right posterior extraperitoneal space the roentgenograms may show little elevation of the diaphragm, although in the lateral view the posterior costophrenic sinus may be obliterated.

In the case of a large subphrenic abscess the roentgenograms may show a patchy area of increased dulness in the lower lobe of the lung, which may be definitely above the lower edge, the result of atelectasis or peribronchial inflammation following immobilization and elevation of the diaphragm. There are frequently increased hilus markings in both lungs, especially in the right.

11. Brown, H. P., Jr.: Subphrenic Abscess, *Ann. Surg.* 93:1075, 1931.

In the case of a subhepatic abscess on the right side the liver may push the diaphragm up with limitation of motion, but there is no gas beneath it.

If the abscess is large there may be an abdominal swelling beneath the liver or in the loin in addition to local tenderness, muscle spasm and rigidity.

Dulness from a subhepatic abscess may extend below the liver, outlining the triangle formed by the falciform ligament, the transverse colon and the costal border, similar to that caused by an abscess of the anterior suprahepatic space. Tenderness and bulging in the right loin occur frequently with a subhepatic abscess as well as with an abscess in the posterior superior space.

Diagnosis is often delayed, even when there are positive roentgenographic signs, owing to the lack of clinical recognition of the condition. When there is gas beneath the diaphragm, physical examination with the patient in the recumbent position may show diminution or absence of hepatic dulness anteriorly and a high axillary dulness which shifts when the patient turns or sits up.

A persisting local tenderness is quite suggestive. A widening of the right side of the chest due to elevation of the lower ribs was observed in case 5, that of an extraperitoneal abscess, without elevation of the diaphragm.

The first symptoms may be either thoracic or abdominal and vary from pleuritis, jaundice, a local swelling and pain or tenderness to those of a spontaneous perforation.

There is often an incubation or quiescent period of a week or ten days, the only symptoms being slight fever and an increased leukocytosis.

After an abscess has formed a defense zone of adhesions, the earlier it is drained the less will be the chances of a fatal issue as a rule. One might suggest delay to permit development of further overlying pleural or peritoneal adhesions, except that rupture, sepsis and pyemia may suddenly develop. Usually after a brief period the abscess increases rapidly in size, and the toxic symptoms become marked. There may be extension of infection through the diaphragm into the pleural cavity, retroperitoneally by way of the lymphatics into the mediastinum or into the peritoneal cavity.

The less frequent intrahepatic abscess is more likely to produce chills and pain referred to the region of the right scapula (Elsberg). A foul odor is more likely to be associated with a subphrenic than with a hepatic abscess. A perinephritic abscess should give rise to some evidence of renal infection, and the intravenous urogram will aid in the diagnosis.

One should consider the possibility of a postoperative subphrenic accumulation of bile due to leakage or injury of the bile ducts, as in the following case.

Recently I removed 3,000 cc. of sterile bile from the right superior anterior subphrenic space, which extended down to the transverse colon. The patient, a 32 year old man, had been operated on three weeks before by another physician, who removed the gallbladder and gallstones. The drain was removed on the second day, and the wound healed. At the operation a segment of the hepatic duct had been excised, and sterile bile had collected beneath the diaphragm with limiting adhesions of the colon. There was little jaundice for the first ten days and slight elevation of the diaphragm. The patient was very weak after the operation and became progressively worse, with little fever and acholic stools. Shortly before drainage, the jaundice became intense, and there was marked elevation of the diaphragm.

After the wound was reopened and the bile drained, I found that the cut ends of the hepatic and common ducts were too indurated and widely separated to suture. A gap of 1 inch (2.5 cm.) was bridged with a rubber tube which extended into the duodenum. Drainage of bile stopped after six weeks.

The patient has gained 30 pounds (13.6 Kg.) and is well after three months.

PROGNOSIS

The prognosis of a subphrenic abscess is always grave, and it is important to operate before the development of sepsis or intrathoracic complications.

The mortality from subphrenic abscesses is somewhat variable but always high (Giertz¹²). Lockwood¹³ reported it to be 33.3 per cent in the cases in which operation was performed and 96.8 per cent in those in which it was not performed. Ochsner and Graves found it to be 32 per cent in their cases of abscess, in which the sources varied, while Bevan¹⁴ stated that it was about 50 per cent in cases of abscess which occurred following appendicitis. Some complications are unavoidable, owing to extensive peritonitis or to a severe original infection.

Aspiration of a subphrenic abscess should be avoided before and if possible at operation, since it is likely to result in empyema or peritonitis, unless adhesions which are difficult to demonstrate are present.

Lockwood found that 41.9 per cent of deaths were due to intrathoracic complications.

Ochsner and Graves found that of 189 patients who were operated on without the pleura or the peritoneum being opened, 21 per cent died; of 305 on whom transpleural drainage was done, 39 per cent died, and of 307 on whom transperitoneal drainage was done, 35.5 per cent died. In 7 cases of their own in which the pleural cavity was opened at operation, the mortality was 85 per cent.

12. Giertz, K. H.: Twenty-Five Years' Experience in the Treatment of Peritonitis, *Ann. Surg.* **104**:712, 1936.

13. Lockwood, A.: Subdiaphragmatic Abscess, *Surg., Gynec. & Obst.* **33**:502, 1921.

14. Bevan, A. D.: Present Status of the Problem of Appendicitis, *S. Clin. North America* **16**:63, 1936.

Barnard reported the development of empyema in 56 of 76 reviewed cases.

A patient with chronic empyema which developed after a drainage operation for subphrenic abscess came under my care recently.

Three months previously this 26 year old man was operated on, and a ruptured appendix was removed four days after the onset of symptoms, with drainage. Ten days later pain developed in the right upper abdominal quadrant, and after five days' observation, including roentgen examination, a subphrenic abscess was drained. The ninth and tenth ribs were resected posteriorly, followed by drainage and healing of the wound. Immediately after the operation the patient suffered from severe pain in the right side of the chest with dyspnea. The pain gradually became worse, and one month later 4 quarts (3.7 liters) of pus was drained from an empyema on the right side. The drainage tube was removed too soon, and the patient came into the hospital quite toxic.

Immediately after the insertion of a catheter into the old sinus and drainage of a large empyema cavity, he obtained relief, but further surgical treatment will be necessary.

There is a need for a safer one stage transcostal drainage operation in which the pleural cavity need not be contaminated. The anterior and posterior subcostal incisions are too far from the small suprahepatic abscesses, which makes it difficult to avoid opening and contaminating the peritoneal cavity.

AUTHOR'S CASES

In my 9 cases all the patients were males. Two deaths occurred, making a mortality of 22.23 per cent. In all the cases the abscess was on the right side, and a drainage operation was performed in each. The ages of the patients varied from 14 to 59, the average being 34. The ages of the 4 patients having perforated ulcers varied from 32 to 59, the average being 42, while the ages of the 4 with appendicitis varied from 14 to 52, the average being 25.

There were 2 cases of perforated duodenal ulcer and 2 of perforated gastric ulcer, in 3 of which operation was performed.

There were 4 cases of acute appendicitis, in only 1 of which had operation been performed, and then for a pelvic abscess.

The length of time from rupture of the viscus or the onset of acute appendicitis to the onset of symptoms of the subphrenic abscess varied from one to sixteen days and it averaged eight days. The symptoms were then present from eight to thirty-nine days and averaged nineteen days before drainage. This was an average of twenty-seven days from the onset of the original infection to operation.

The temperature during most of the course of the abscess was rarely over 102 F., but before operation there was usually a steplike rise, with increased toxemia and a slight drop in the white cell count. The number of white cells varied from 7,000, a count made after per-

Data on the Author's Nine Cases of Subphrenic Abscess

Case	Sex	Age, Years	Source of Abscess and Days Before Drainage	Previous Operation	Time Between Onset of Abscess to Source of Symptoms, Days	White Blood Cell Count	Location of Abscess in Space; Contents of Abscess	Method of Drainage	Complications and Result
1	M	59	Perforated duodenal ulcer; 39	0	0	21,900	Right superior anterior space; 2,000 cc. + gas	Transcostal route, 10th rib; extrapleural method	Cured; sinus 5 mo.
2	M	46	Perforated gastric ulcer; 22	+	11	30,900	Right superior anterior space; 2,000 cc.	Transcostal route, 10th rib; extrapleural method	Died; moribund at operation; bilateral bronchopneumonia
3	M	32	Perforated gastric ulcer; 46	+	18	10,240	Right superior anterior space; 300 cc.	Transcostal route, 9th rib; extrapleural method	Cured 1 yr. and 9 mo.; sinus 2 mo.
4	M	32	Perforated duodenal ulcer; 15	+	6	25,150	Right superior anterior space; 500 cc. + gas	Transcostal route, 8th rib; author's extrapleural method	Cured 1 yr.; sinus about cartilage; resected 4 mo. later
5	M	17	Acute appendicitis; 35	0	7	20,530	Right extrapleural superior space; 500 cc. Staph. albus on culture	Posterior transcostal route, 12th rib	Cured; sinus 2 mo.
6	M	14	Appendicitis with perforation; 17	0	9	16,300	Right superior posterior space; 1,000 cc.	1. Transcostal route, 10th rib; exploration of peritoneal cavity extrapleurally 2. Posterior subcostal route, 12th rib	Cured; pelvic abscess drained by rectum before symptoms of subphrenic abscess developed
7	M	18	Appendicitis with perforation; 15	0	6	20,900	Right superior posterior space; 800 cc.	Posterior subcostal route, 12th rib	Died 10 days postoperatively; bronchopneumonia of left lung and empyema
8	M	52	Appendicitis with perforation; 23	0	9	14,400	Right superior posterior and right inferior spaces; 3,000 cc.	Posterior subcostal route, 12th rib	Cured; sinus 2 mo.
9	M	42	Perforated gallbladder; 35	0	10	7,000	Right inferior and part of right superior anterior spaces; 75 cc.; colon bacilli on culture	Anterior subcostal route; right rectus incision; cholecystectomy and drainage	Cured 3 yr.; sinus 3 wk.

foration of a gallbladder, to 30,900, a count made twenty-two days after an operation for a perforated gastric ulcer, which was associated with bilateral pneumonia and terminated fatally. The average count made just before drainage was 18,900. With one exception, there was a higher white cell count in the cases in which the abscess was large. In this case the white cell count was 14,400 and there was 3,000 cc. of pus in the abscess cavity twenty-three days after the onset of appendicitis which was not treated surgically.

The symptoms suggesting a subphrenic abscess were first noted in the side of the chest in 4 cases, in 3 after a perforated ulcer and in 1 after appendicitis, while in 5 cases the first symptoms were abdominal, in 1 after an ulcer, in 3 after appendicitis and in 1 after perforation of the gallbladder.

The correct diagnosis was made before operation in 8 cases, or 88 per cent.

The subphrenic abscess was in the right anterior superior space in 4 cases, in all of which it followed a perforated ulcer. In 4 cases the abscess followed acute appendicitis; it was located in the right extra-pleural superior space in 1 and involved the right posterior superior space in the other 3. In one of the latter it extended forward to the anterior abdominal wall into the inferior space and contained 3,000 cc. of pus.

In the case in which there were two separate perforations of the gallbladder there were two abscess cavities, one inferior to the liver and a smaller one just above the edge of the liver.

The size of the abscess varied from 75 to 3,000 cc., the average size being 1,040 cc. There was little difference in the size of the abscesses which developed following a perforated ulcer and of those which occurred after acute appendicitis.

There was gas in two abscess cavities, or 22 per cent, both of which occurred after perforated ulcers. The pus had a foul odor in 3 cases. *Staphylococcus albus* was cultured from the pus of an abscess which occurred after appendicitis, and colon bacillus was cultured from the pus of the one which occurred after a perforated gallbladder.

In 1 case in which abscess followed a perforated ulcer there was extensive bronchopneumonia on each side, and the patient was moribund at operation.

The other death was due to involvement of the opposite lung with pneumonia and empyema ten days after operation.

Most of the operative wounds drained from one to three months, but in 2 instances the period of drainage was longer and there were no recurrences.

The persistence of the high diaphragm laterally after a month of drainage, as shown by roentgenograms in cases 6 and 8, was probably

due to extensive adhesions, which explains the slow obliteration of these abscess cavities.

There have been no complaints as a result of the abscess and operation.

There was a recurrence of symptoms of ulcer in 1 case a year later, which necessitated medical treatment.

OPERATIVE TREATMENT

Drainage of a subphrenic abscess may be obtained through one of four regions, depending on the location and size of the abscess. The transcostal route may be chosen either anteriorly in the axillary line or posteriorly through the twelfth rib. The subcostal route may be used anteriorly through the abdomen or posteriorly beneath the twelfth rib and the level of the pleural reflection.

If the abscess is localized above the liver in the anterior superior space and beneath the dome of the diaphragm, extrapleural drainage should be established by resection of a rib in the axillary line directly above or as close to it as possible.

If an abscess is small, one may choose to resect the eighth rib, while for the larger abscesses, which extend lower, the ninth or tenth rib should be resected, since there is a wider extrapleural part of the diaphragm in this region and drainage should be established both as low and as posteriorly as feasible.

Elsberg has described the transcostal operation with resection of two ribs, the ninth and the tenth.

He established drainage through the diaphragm below the pleural reflection when it was possible, while in other cases he first obliterated the pleural cavity around the operative area by a circular suture between the pleural layers.

Occasionally the pleural cavity may be obliterated in this region by adhesions, or the pleural reflection may be elevated by pressure from the abscess (Boeckel¹⁵).

Lilienthal¹⁶ and Parijsky¹⁷ have been able to mobilize the costophrenic reflection of the pleura and push it upward, but Brown stated that this was not practical owing to frequent adhesions. It also necessitates the resection of two or more ribs, and the pleura may be torn and the pleural cavity contaminated.

While most surgeons attempt to obliterate the pleural cavity either by a circular suture or by a gauze pack, these procedures are not always satisfactory, even if the abscess is drained a few days later, as shown

15. Boeckel, cited by Ochsner and Graves.⁴

16. Lilienthal, H., in discussion on Ochsner and Graves,⁴ p. 990.

17. Parijsky, cited by Ochsner and Graves.⁴

by frequent secondary empyema and high mortality (Elsberg and Ochsner and Graves).

Immediate drainage is usually advisable, since a few days' delay may result in sepsis and pulmonary complications.

In 4 of my cases the abscess was in the right anterior superior space and either localized beneath the dome of the diaphragm or extended well forward and laterally.

In cases 1, 2 and 3 I resected either the ninth or the tenth rib in the axillary line and opened the abscess through the diaphragm, below the pleural reflection, without opening the pleural or the peritoneal cavity (fig. 1 *B* and *B'* and fig. 2).

Since there is no test for determining the level of the costophrenic reflection, one cannot always avoid opening the pleural cavity in a trans-costal operation unless adhesions are present or the pleural reflection is high.

In case 4 there was a relatively small localized abscess under the dome of the diaphragm (fig. 3). The eighth rib was resected in the anterior axillary line, and the pleural cavity, which extended quite low, was opened (fig. 1 *C*). A delay of several days before drainage of the abscess would have been necessary if the usual obliterative methods of suture or packing of the pleural cavity had been used, and there would have been the additional danger of empyema.

An original and simple method was devised to obliterate the pleural cavity and at the same time to make an extrapleural area of the diaphragm which could be safely incised, with immediate drainage of the abscess (fig. 1 *C'* and *D*).

The patient (case 4), a man aged 32, entered the hospital on June 13, 1935, complaining of severe pain in the upper part of the abdomen for three hours associated with vomiting. There were no previous symptoms, except that during the last two weeks he had noticed some gastric distress from one to two hours after meals, which was relieved by rest.

The past history was unimportant, except for an operation for removal of the appendix several years previously.

Physical examination revealed marked rigidity over the entire abdomen and a decreased area of hepatic dullness. The white cell count was 9,300.

An emergency operation was performed six hours after the onset of symptoms, and a perforated ulcer of the duodenum was sutured, with aspiration of free fluid.

Convalescence was good until the tenth day, when the patient had a temperature of 101 F. On the eleventh day there was some pain on the side of his chest and a leukocyte count of 28,150. On physical examination there were diminished breath sounds posteriorly and a lack of respiratory excursion of the diaphragm but no râles. With the patient in the recumbent position an area of high axillary dullness and one of tympany were noted over the region of the liver anteriorly. When he turned to either side the area of dullness and that of tympany shifted, suggesting a subphrenic abscess containing gas.

Fluoroscopic examination and roentgenograms showed an abscess cavity containing gas under the right side of a high fixed diaphragm (fig. 3).

Operation was performed on June 28, 1935, my original technic of transcostal extrapleural drainage being employed.

A local anesthesia was used, and about 2 inches (5 cm.) of the eighth rib was resected as low as possible in the anterior axillary line. The pleural reflection was so low that it was impossible to push it up without resecting another rib and perhaps accidentally opening the pleural cavity. A longitudinal incision was made through the costal pleura in the bed of the resected rib, starting about 1 cm. from the upper end (fig. 1 *C'*). This pleural incision was continued downward to the pleural reflection and then upward through the diaphragmatic pleura to a point below the beginning of the anterior incision. The two edges of the diaphragmatic pleura with a thin layer of the underlying muscle were then dissected laterally. The lower edge of the pleura was widely approximated and sutured with two rows of fine catgut, without tension, to the overhanging free edge of the costal pleura and intercostal muscles, completely obliterating the pleural cavity. This suture line was completely covered with a narrow strip of gauze impregnated with petrolatum, which was sutured securely over it with fine catgut (fig. 1 *D*).

This procedure, with resection of only one rib, provided an extrapleural U-shaped diaphragmatic area about 3 cm. long and 1.5 cm. wide, which was entirely satisfactory for drainage of the underlying abscess. A small aspirating needle was inserted through this extrapleuralized portion of the diaphragm, and an abscess containing about 500 cc. of pus was located and opened by means of a small incision.

Convalescence was uneventful, with no symptoms of pleuritis, and the patient left the hospital one month later with a small amount of drainage. The cavity healed after about two months, but a sinus persisted at the lower end of the wound around the overlying cartilage. This was resected three months later, and the patient has had no further complaints.

On examination one year and nine months after operation the lungs showed no pleural thickening. The patient had regained his normal weight and had been working steadily for over one year.

For the suprahepatic abscess, one rubber tube is usually sufficient for drainage. For the large abscess associated with marked toxemia, a gradual decompression may be advisable.

The drainage tube should be sutured to the skin and daily irrigation employed. The size of the cavity should be determined from time to time by the injection of fluids or by roentgenographic visualization, and the tube should be shortened occasionally as obliteration occurs.

The abscesses of the subhepatic and posterior spaces may be drained more freely, but one should avoid extensive manipulation, and the forceful rib-spreading exploration of Lockwood in order to locate multiple cavities should be rarely necessary.

If a subphrenic abscess points in the upper part of the abdomen, extending forward either from the right superior anterior space or from the subhepatic space, it may be drained through an anterior abdominal incision.

The larger of these abscesses are limited medially by the falciform ligament, below by the transverse colon, which becomes adherent to the anterior wall, and laterally by the costal arch, which forms a bulging triangle of dullness in the upper portion of the abdomen.

The abdominal route was used in a majority of all cases reported by Gatewood.¹⁸ However, there is danger of opening the general peritoneal cavity unless the abscess is walled off by adhesions well below the incision. Either a high rectus or an oblique subcostal incision may be used to drain an abscess pointing in this region.

The subcostal approach of Clairemont and Meyer¹⁹ is intended to drain a high-lying suprahepatic abscess extraperitoneally. This incision extends parallel to the costal margin down to the peritoneum, which may be separated from the diaphragm by the finger without tearing it until the abscess is reached.

In case 9 of my series, after a perforation of the gallbladder from stones abscess cavities were localized beneath the liver and between it and the abdominal wall. The general peritoneal cavity was opened through a right rectus incision and both cavities opened and found to contain gallstones. The markedly diseased and perforated gallbladder, which contained other stones, was removed, with drainage anteriorly, and recovery resulted.

A large subhepatic abscess may point both posteriorly and anteriorly, but the posterior drainage route beneath the twelfth rib into Morison's pouch is usually easier and safer and provides better drainage than the anterior route.

If the abscess is localized in the upper part of the posterior superior space or above that in the extraperitoneal space, the twelfth rib may have to be dislocated upward, or resected as advocated by Ochsner and Graves, and the peritoneum separated from the under-surface of the diaphragm until the abscess is reached. In either instance, but especially in the latter, the costophrenic sinus may be found obliterated with the abscess directly against the lower ribs.

In cases 6, 9 and 8 the right posterior superior space was involved, with bulging in the loin. In case 6, in which the bulging extended well forward, the tenth rib was resected, the peritoneal cavity was explored through the extrapleural part of the diaphragm and the abscess was opened well back under the liver. A second small incision was made posteriorly beneath the twelfth rib directly into the abscess cavity, and drains were inserted. The peritoneal cavity around the transcostal extrapleural incision was walled off with an iodoform gauze pack, and the patient had an uneventful convalescence.

18. Gatewood: Subphrenic Abscess, *Am. J. M. Sc.* **180**:398, 1930.

19. Clairemont, P., and Meyer, M.: Erfahrungen über die Behandlung der Appendicitis, *Acta chir. Scandinav.* **60**:55, 1926.

In case 7 the abscess bulged only in the loin, while in case 8 it pointed both in the loin and anteriorly, with a large triangle of dulness. In each case the abscess was drained posteriorly by an incision beneath the twelfth rib, but in spite of this in case 7, one of extensive primary peritonitis, a fatal suppuration developed in the opposite lung, associated with empyema.

Posterior drainage beneath the twelfth rib is accomplished by the following technic:

A transverse incision is made posteriorly at the level of the spinous process of the first lumbar vertebra, which will avoid the danger of

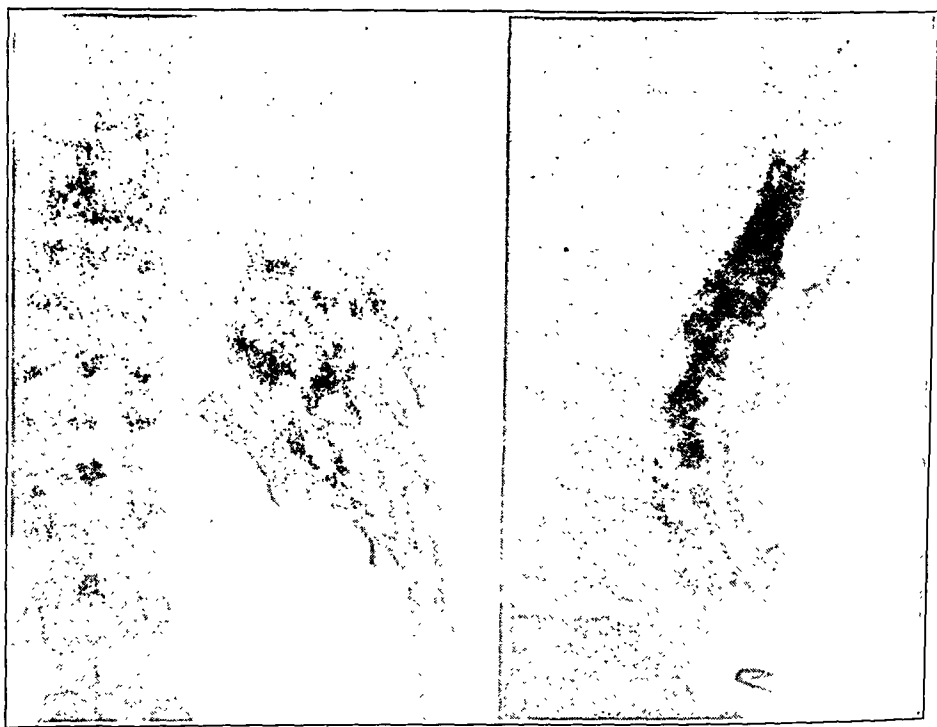


Fig. 4 (case 5).—Roentgenographic visualization of the right extraperitoneal abscess cavity ten days after resection of the twelfth rib and drainage. Elevation of the diaphragm was not present before operation.

opening the pleural cavity (Cunningham). The latissimus dorsi and the external oblique muscles and the deep fascia just lateral to the erector spinae muscles are split, and exploration for the abscess is made by blunt dissection beneath the peritoneum. Large abscesses extending downward and into the posterior superior pouch of Morison are easily palpated and opened into directly beneath the incision, and it is undesirable and rarely necessary to aspirate for diagnosis. Two large fenestrated rubber tubes, which are not too stiff or too long, are inserted for drainage and sutured to the skin with silkworm gut, and the wound with its separated muscle fibers is left open.

High-lying abscesses behind the liver may be opened by blunt separation of the peritoneum upward; occasionally a rib resection may be necessary, unless Bevan's method of forcefully dislocating the twelfth rib upward provides enough exposure.

In case 5 the abscess was limited to the right extraperitoneal space posterior to the liver and above the level of the twelfth rib. The sub-costal approach was made, and the inferior surface of the liver was palpated without opening the peritoneum or locating the high-lying abscess. The edges of the skin and muscles were then retracted higher up, and the twelfth rib was resected. The lower edge of the abscess, which contained 500 cc. of pus, was opened posterior to the liver in the bed of the resected twelfth rib and drained with two large rubber tubes (fig. 4).

In reviewing the operative procedures in my cases, 3 of the 4 abscesses of the superior anterior space were easily drained through the extrapleural portion of the diaphragm by the anterior transcostal operation. In the fourth case the pleural cavity was satisfactorily excluded, and extrapleural drainage was established by an original procedure.

Resection of the twelfth rib by the posterior route was necessary in case 5, in which the abscess was in the right extraperitoneal space.

In case 9 the peritoneal cavity was opened anteriorly.

In 3 cases an abscess of the posterior superior space pointed in the loin, and drainage was done posteriorly beneath the twelfth rib.

CONCLUSIONS

1. One should make every effort to diagnose a subphrenic abscess from the first symptoms, especially when the patient fails to improve satisfactorily after an attack of appendicitis, a perforated ulcer or any abdominal infection or operation.

The onset of symptoms is usually within a week or ten days after the original infection but may develop weeks or months later. Repeated comparative examinations may be necessary for diagnosis.

A quiescent period may precede the onset of symptoms, but no time should be lost before establishing drainage, because the sudden development of sepsis and pulmonary complications is the major factor in the high mortality.

2. Complications may be largely avoided by early drainage with the method most suitable to the location and size of the abscess.

3. An original transcostal operation is reported by means of which immediate extrapleural transcostal drainage may be established.

INJECTION OF ETHER INTO THE BILIARY TRACT AS TREATMENT FOR CHOLEDOCHOLITHIASIS

J. G. PROBSTEIN, M.D.
AND
CLARENCE T. ECKERT, M.D.
ST. LOUIS

In recent years great strides have been made in the study of the chemistry and physiology of the biliary tract. This increase in knowledge, however, has not altered the position pathologic conditions of the biliary tract hold as formidable opponents of the surgeon's diagnostic and technical skill. In reviewing causes for some of the unsatisfactory surgical results, we find stones in the common duct to be one of the most frequent offenders. The simple case of a large stone high in the common duct, with a typical history of obstruction of the biliary tract, of course, offers no difficulty. However, the small stones low in the common duct frequently remain undiagnosed before and even during operation. Many observers have called attention to the symptomatic silence of this condition. Clute,¹ in reviewing seventy-nine cases of stones in the common duct, found that there was no history of jaundice in twenty-nine. Lahey² found that in 39 per cent of his cases of stones of either the common or the hepatic ducts there was absence of jaundice; he called particular attention to the frequency with which small stones low in the duct were overlooked at operation. From time to time many articles have appeared advocating different procedures or instruments for discovering and removing these stones. Nevertheless, in this regard the surgical world is still far from Utopia, and the present status was aptly described by Clute and Swinton³ when they stated that "as yet we have no means at our command which will determine positively after exploration of the common duct that every stone has been removed." Besides failing to guarantee removal of the stones, exploration of the common duct definitely increases the mor-

From the David May Surgical Research Fund of the Jewish Hospital, and the Surgical Department of Washington University School of Medicine.

1. Clute, H. M.: Common Duct Stones Without Jaundice, *S. Clin. North America* **11**:261-269 (April) 1931.

2. Lahey, F. H.: Incidence and Management of Stones in Common and Hepatic Ducts, *Ann. Surg.* **98**:644-649 (Oct.) 1933.

3. Clute, H. M., and Swinton, N. W.: Exploration of Common Duct in Gall-Stone Surgery, *Surg., Gynec. & Obst.* **59**:906-912 (Dec.) 1934.

tality for operations on the biliary tract. Consequently, any method which would obviate this procedure and still lead to the removal of the stone could be counted as a distinct advance.

Since the discovery by Vollisnieri⁴ in 1722 that gallstones were soluble in alcohol and turpentine, innumerable ideas have been presented for the use of lipoid solvents in the treatment of biliary stones. Many years ago (1908) Wright⁵ reported a case in which stones were impacted into a mass in the common duct and could be removed only after the injection of 1 drachm (3.7 cc.) of turpentine directly on the impaction. In 1932 Pribram⁶ reported a case of cholelithiasis, in which the stone was tightly lodged in the papilla of Vater, with successful treatment by the daily injection of ether into the common duct. Later (1935) he⁷ reported five cases of "sepsis and cholemia" in which stones in the common duct were also successfully treated by his method, which consisted of the insertion of a tube into the common duct down to the obstruction and the daily injection of "several cubic centimeters of ether" on the stones. In addition to the ether, he mentioned irrigations with sodium chlorate. From time to time he checked the progress of the obstruction fluoroscopically after the injection of iodized oil into the common duct.

The purpose of our work was, first, to investigate the effects of ether, a lipoid solvent, as injected directly into the biliary tract with obstruction of the common duct and, second, to determine whether or not ether would dissolve the ordinary stones under conditions simulating incarceration in and blockage of the common duct.⁸

EXPERIMENTAL METHODS

Mongrel dogs weighing from 15 to 17 Kg. were used in this work. With an animal under ether anesthesia, we tied the common bile duct with two silk sutures as closely as possible to the duodenal wall and cut the duct between the sutures. The head of a small mushroom catheter was fixed into the gallbladder by means of a purse-string suture, the free end of the catheter being brought out of the abdomen by means of a stab wound. The catheter was allowed to drain continuously into voluminous sterile dressings. Several days postoperatively, when the dog appeared and acted normally, the daily injection of from 3 to 6 cc. of ether into the catheter was begun. The only pressure exerted on the ether during the injections was

4. Vollisnieri, cited by Sherwood, K. K.: Historical Sketch of Cholelithiasis, Northwest Med. 30:335-340 (July) 1931.

5. Wright, G.: The Value of Turpentine in Gall-Stone Surgery, Brit. M. J. 2:1808, 1908.

6. Pribram, B. O.: Zur Beseitigung eingeklemmter Choledochuspapillensteine, Deutsche med. Wchnschr. 58:1167-1169 (July 22) 1932.

7. Pribram, B. O.: New Methods in Gall-Stone Surgery, Surg., Gynec. & Obst. 60:55-64 (Jan.) 1935.

8. We were unable to dissolve the most ordinary bilirubin calcium stones rapidly by mixing them with ether, as described by Pribram. The process usually took a period of days.

that minimal amount necessary to expel the fluid from the glass syringes used for the instillations. Sterile technic was used at all times. While this method of injection was being studied, we noticed marked decreases in the total output of bile. After much difficulty, a satisfactory method was evolved for studying the output of bile, which at the same time permitted us to make the necessary injections. Here, too, the common duct was doubly tied and severed in the foregoing manner. For drainage we used a 10 cm. glass tube with a 1.5 cm. open bulb at each end. One bulbous tip was inserted into the gallbladder and held in place by a purse-string suture. The other end was brought to the outside by forcing it through a small stab wound in the wall of the right side of the abdomen. The external bulbous tip of the tube was sufficient to prevent it from being drawn into the abdomen by respiratory or other movements. The tubing within the abdomen was covered with omentum. To the external bulb of the drainage tube was attached one arm of a T tube, and to another arm of the T tube was connected a balloon for collecting the bile. A screw clamp on the remaining arm of the T tube converted the apparatus into a closed system, so that the biliary drainage was collected in the balloon. To empty the balloon the screw clamp was removed from the free arm of the T tube and placed on the arm connected to the glass drainage tube, thus enabling us to express the bile from the balloon without forcing the fluid back into the biliary tree. To instill the ether the clamp was then placed on the arm of the T tube connected to the balloon, and the drug could be injected through the open arm of the T tube into the gallbladder without entering the collecting bag. After the injection the clamp was replaced on the free arm of the T tube and the bile allowed to collect for another twenty-four hours. All of the external collecting apparatus was held in a circular enameled metal cup, which was in turn supported by a binder of stout canvas. Pockets, which exactly fitted the cups, were tailored into the binders, so that when the latter were tightened the edges of the cups made no undue pressure on the dog's abdomen. The whole apparatus was well tolerated by all the dogs and did not seem to interfere with their normal activity. The injections of ether were not started until a normal output of bile had been maintained for three days. Animals which did not fully recover from the operation or those showing any signs of infection were discarded. The usual diet of meat and water was not varied throughout the experiment. The dogs were taken from their cages each day for fifteen minutes of exercise. When an animal died or was killed because of poor condition, a postmortem examination was done, and sections for microscopic study were taken from various parts of the biliary tract and liver. Tissue was also taken from the pancreas, spleen and kidneys.

To determine the solubility of the usual stone in the biliary tract under conditions simulating incarceration within and blockage of the common bile duct, we placed various stones in pieces of rubber tubing so as to just block the lumen of the tube. The piece of tubing containing the stone was then connected to an inverted bottle partially filled with ether. In order to maintain atmospheric pressure within the bottle at all times, a glass U tube was also placed through the stopper with both arms above the level of fluid. The bottle was agitated daily so as to place "new" ether in contact with the stone.

EXPERIMENTAL RESULTS

Ether was injected into the biliary tract in eleven dogs, and in six of these the total daily output of bile was checked as described. All of the dogs objected strenuously to the injections. This reaction usually subsided in from two to four

minutes but on several occasions was prolonged into what seemed to be a convulsive seizure. The increased pressure within the biliary tract, due to evaporation and movement, caused variable amounts of ether to be expelled. In the dogs with the closed system of biliary drainage, the screw clamp was never replaced on the free arm of the T tube until the ether was no longer being expelled. After the injection dressings were applied, and the animals were removed from the boards and allowed to walk. More often than not a dog would be unable to walk normally, assuming a drunken reeling gait. When this reaction occurred, the dog also became nauseated and vomited. This disturbance in walking usually lasted from ten to fifteen minutes, but the nausea and vomiting persisted for from one half to two hours. Once the injections began, all of the dogs became listless, had meager appetites, appeared extremely weak and lost weight.

All of the dogs (six) on which the twenty-four hour output of bile was measured showed a marked decrease after the instillation of ether. The normal output varied from 130 to 160 cc. per twenty-four hours. After only three or four instillations we could collect but 40 to 50 cc. a day. This decrease in the output of bile was progressive, so that in the three dogs which received the greatest number of injections (eight, eleven and fourteen) there was a complete stoppage of biliary secretion. The eight remaining animals either died or were in such poor condition that they were killed with ether before receiving as many as eight injections.

Clinical signs of jaundice were noted in three of the dogs. These were observed in animals which survived longest and which had also ceased to secrete bile.

At autopsy none of the animals had free bile in the peritoneal cavity, though in one a small amount of a blood-tinged serous fluid was found. Grossly the liver appeared normal except in the three dogs exhibiting jaundice. In these the liver was firmer and definitely bile stained on section. In two animals the bulbous tip of the glass tube which had been maintained in the gallbladder was found to be covered with a layer of fine concretions. In one the common bile duct was thought to be definitely thickened. No gross changes were noted in any other portion of the biliary tract or in any of the other abdominal or thoracic viscera.

Microscopically, the ether seemed to cause a progressive destruction of the mucosa lining the biliary tract and gallbladder. At first the columnar cells became edematous and pale staining and had much lighter nuclei than normally. The cytoplasm then became filled with small granules, the nuclei became still lighter staining and finally the cells appeared to disintegrate and slough. The microscopic changes in the liver were definite and in some instances marked but did not seem to be quantitatively related to the amount of ether injected. Likewise, the hepatic pathologic process gave no clue as to the amount of bile secreted nor as to the general condition of the animal.

The hepatic parenchymal cells were for the most part edematous, and the cytoplasm took an abnormally light stain. The nuclei seemed normal except in those cells which had undergone a fine granular degeneration. In these instances the nuclei were pale. In the dog which had received fourteen injections the liver showed scattered areas of complete destruction. All of the sections showed marked engorgement of the capillaries and slight thickening of the arterial walls. The Kupffer cells were numerous and contained phagocytosed granules, the latter being especially marked in the animals which were jaundiced. These microscopic changes in the liver were present diffusely throughout the lobule and did

not seem to vary with proximity to the bile duct or blood vessel. The pathologic process was slightly more marked, however, in the sections taken at or near the hilus than in those taken from the periphery.

Sections of the spleen, pancreas and kidneys were normal in all dogs except one, which showed many hyaline casts in the renal tubules.

Attempts to dissolve stones placed in rubber tubing in the manner described were unsuccessful after fifteen days of constant contact with the ether. One stone was left in place for three months without leakage of ether past the site of incarceration and obstruction.

COMMENT

The most interesting and noteworthy result of these experiments was the rapid decline of the dogs immediately after the beginning of the injections of ether. The sudden decrease in the total output of bile can be accounted for only by injury to the liver parenchyma, it being conceded that the hepatic cell is the source of bile salt formation. This result, however, is not unusual, for Whipple and Smith⁹ found that when small amounts of chloroform, another lipoid solvent, were administered by mouth a "marked depression in the bile salt output" resulted. Thus one would expect an even greater decrease in the total output of bile when, as in the present experiment, the toxic material came in direct and immediate contact with the liver parenchyma. That the injected ether actually did enter the hepatic biliary tree was deduced from the fact that from 3 to 5 cc. of a suspension of barium sulfate injected into the drainage tube was seen to spread up into the liver.

The convulsive seizures, rapid loss of weight and extreme listlessness of the animals point to another expected result, namely, a disturbance in glycogenesis, one of the major functions of the liver. King¹⁰ called attention to the frequent reports of convulsions under ether anesthesia which have appeared in English literature since 1925. Sears¹¹ expressed the belief that this reaction is a result of hypoglycemia due to a depleted reserve of glycogen and has advocated as treatment the intravenous administration of concentrated solutions of dextrose. Evans, Tsai and Young,¹² working with cats, found that ether anesthesia lowers the glycogen content of the liver from 15 to 20 per cent in from five to six minutes, with a subsequent drop to less than 50 per cent in one hour, after which the fall is checked. Even though ether anesthesia is accompanied by hyperglycemia, which Can-

9. Whipple, G. H., and Smith, H. P.: Bile Salt Metabolism: Liver Injury and Liver Stimulation, *J. Biol. Chem.* **89**:727-738 (Dec.) 1930.

10. King, H. J.: Convulsions Under Ether Anesthesia, *Am. J. Surg.* **30**: 182-184 (Oct.) 1935.

11. Sears, J. B.: Late Ether Convulsions: Report of Two Cases, *J. A. M. A.* **100**:1150-1152 (April 15) 1933.

12. Evans, C. L.; Tsai, C., and Young, F. G.: Behaviour of Liver Glycogen in Experimental Animals; Methods: Effect of Ether and Amytal, *J. Physiol.* **73**: 67-80 (Sept.) 1931.

tarow and Gehret¹³ stated they believed to be due to an increased hepatic glycogenolysis, Major and Bollman¹⁴ found that prolonging such anesthesia caused a marked decrease in the skeletal glycogen. Unfortunately no studies on the chemistry of the blood or tissue glycogen were done in this work. Also interesting would have been a quantitative analysis of the amount of ether present in the various tissues and a comparison of the results with those of Gettler and Siegel,¹⁵ who found that the ether in tissues is "always higher than 0.3 cc. in 500 Gm." in cases in which the patient died under full ether anesthesia or as the result of an accidental overdose. However, as explained previously, histologic evidence of damage due to ether in the spleen, pancreas or kidneys was entirely lacking except in one dog, which showed several hyaline casts within the kidney tubules.

The development of jaundice in three of our dogs was in keeping with the same findings after the administration of other lipid solvent hepatic toxins, such as chloroform and carbon tetrachloride. The cause of this jaundice, as suggested by Mann and Bollman,¹⁶ "appears to be due in part to hepatic injury and in part to excessive formation of bilirubin which cannot all be eliminated by the injured liver." As mentioned before, the phagocytosis of the excess pigment by the Kupffer cells was especially marked in the jaundiced dogs.

Owing, no doubt, to the relatively short period of observation, sections of the liver failed to reveal other pathologic changes, such as fatty degeneration, cirrhosis or regeneration.

The essential pathologic changes in the extrahepatic biliary tract and the larger bile ducts in the liver were those of necrosis and sloughing of the epithelial lining. There was a noted absence of any inflammatory changes, with only an occasional submucous infiltration of small round cells. Here again the short period of observation precluded the possibility of regeneration of this destroyed mucosa. Under favorable conditions the epithelium lining the ducts is capable of regeneration,¹⁷ and in cats Stewart and Lieber¹⁸ found that ligation of the

13. Cantarow, A., and Gehret, A. M.: Ether Hyperglycemia, with Especial Reference to Hepatic Disease, *J. A. M. A.* **96**:939-941 (March 21) 1931.

14. Major, S. G., and Bollman, J. L.: Effect of Ether and Iso-Amyl-Ethyl Barbiturate (Amytal) Anesthesia on Glycogen Content of Skeletal Muscle, *Proc. Soc. Exper. Biol. & Med.* **29**:1109-1111 (June) 1932.

15. Gettler, A. O., and Siegel, H.: Isolation of Ether from Human Tissues, *Arch. Path.* **17**:510-515 (April) 1934.

16. Mann, F. C., and Bollman, J. L.: Jaundice: Review of Some Experimental Investigations, *J. A. M. A.* **104**:371-374 (Feb. 2) 1935.

17. Halperin, G.: Regenerative Capacity of the Extrahepatic Biliary Tracts, *Surg., Gynec. & Obst.* **56**:868-883 (May) 1933.

18. Stewart, H. L., and Lieber, M. M.: Ligation of Common Bile Duct in Cat, *Arch. Path.* **19**:34-36 (Jan.) 1935.

common duct caused an enormous proliferation of the mucosa of the larger ducts, particularly after the tenth day.

The almost immediate distress of the animals after the injection of the ether was due partially, we think, to the irritating character of the substance and probably more to the rise in pressure within the biliary tract resulting from the evaporation of the ether at body temperature. Pribram⁶ warned against the injection of more than 2 to 3 cc. at a time, stating that larger quantities produced pain. Zollinger¹⁹ distended the common duct in man by means of a balloon inserted during laparotomy and found that an increase of pressure within the duct led to severe pain, nausea, vomiting and respiratory difficulty. This description accurately portrays the condition of our animals soon after the instillation of ether. Sheldon,²⁰ when injecting skiodan into the common duct for visualization, noticed that the patient complained of precordial anginal pain when too great pressure was used.

The deposit of calcium on the glass tubes draining the gallbladder is an interesting but common finding. Hospers²¹ cited several workers who before the turn of the century reported the deposition of calcium on foreign bodies placed within the gallbladder. This condition may have been due, as is frequently the case in calcification of the wall of the gallbladder,²² to the mobilization of the calcium by the blood cells, present in this instance as a result of the operative procedures. A more plausible explanation, however, is that the deposition of calcium was due to the continued irritation of a foreign body, the glass tube in this case. Moynihan²³ gave particular credence to this factor in his work dealing with the deposition of a layer of calcium on gallstones. By making roentgenograms of operative specimens, he found that with few exceptions the smaller stones were translucent, but as a stone became larger a thin radiopaque layer of calcium formed on its surface. It was also his opinion that the calcium deposited more rapidly on an impacted stone.

This covering of calcium is, we think, the explanation of our inability to dissolve an apparently soluble stone by placing it in constant contact with ether as described before. Though solitary stones have

19. Zollinger, R.: Observations Following Distension of Gall-Bladder and Common Duct in Man, *Proc. Soc. Exper. Biol. & Med.* **30**:1260-1261 (June) 1933.

20. Sheldon, L. B.: Clinical Study of Biliary Secretion in Case Presenting Completely Obstructed Common Duct, *J. A. M. A.* **104**:915-916 (March 16) 1935.

21. Hospers, C. A.: Experimental Production of Gall-Stones, with Review of Literature, *Arch. Path.* **14**:66-78 (July) 1932.

22. Davis, J. E., and Bookmyer, R. H.: Intramural Calcification of Gall-Bladder, *Ann. Surg.* **96**:413-417 (Sept.) 1932.

23. Moynihan, B.: Mitchell Banks Memorial Lecture on Gallbladder and Its Infections, *Brit. M. J.* **1**:1-6 (Jan. 7) 1928.

been found to contain from 98 to 99 per cent cholesterol, the common mixed or combination gallstones were found to have an average cholesterol content of but 94 per cent.²⁴ Thus while the calcium content is relatively small, its position as an enveloping layer may easily be sufficient to prevent solution of the stones by lipid solvents.

Thus far we have discussed features concerning this method of treatment as brought to light by our experimental work. There are other points to bear in mind before injecting a lipid solvent into the biliary tract. Ever since Graham²⁵ first described it, the occurrence of hepatitis has been accepted as a "constant accompaniment of cholecystitis." Since we also think of stones as evidence of an antecedent disturbance of the gallbladder or the liver,²⁶ in any case in which surgical intervention for stones is necessary there is, or has been, infection of the liver, and there may be a more dangerous reaction to a toxic agent than is expected or is desired.

Another theoretical consideration is the possibility of the ether causing pancreatitis. That this is commonly possible mechanically was demonstrated by Cameron and Noble²⁷ on postmortem experimentation. They inserted 3 mm. calculi into the terminal portion of the choledochus and raised the intraductal pressure to 100 mm. of water. It was found that fluid entered the pancreatic duct in sixty-six of one hundred cases, and in seventy-four of the one hundred there was an ampullary communication between the choledochus and the duct of Wirsung. They also called attention to the fact that during retching or vomiting the pressure within the common duct usually rose to 350 mm. of bile, but might go as high as 1,000 mm. These findings are in striking accord with those of Wangenstein and his co-workers,²⁸ who reported that in 69.8 per cent of their cases of acute pancreatitis the condition was associated with stones or disease of the gallbladder. Since in our experiment the common duct was severed just outside the duodenum, we were unable to check these findings.

24. Pickens, M.; Spanner, G. O., and Bauman, L.: Composition of Gall-Stones and Their Solubility in Dog Bile, *J. Biol. Chem.* **95**:505-507 (March) 1932.

25. Graham, E. A.: Hepatitis: A Constant Accompaniment of Cholecystitis, *Surg., Gynec. & Obst.* **26**:521-537 (May) 1918.

26. Bortz, E. L.: Restoration of Biliary Function, *M. J. & Rec.* **136**:244-248 (Sept. 21) 1932.

27. Cameron, A. L., and Noble, J. F.: Reflux of Bile up the Duct of Wirsung Caused by an Impacted Biliary Calculus, *J. A. M. A.* **82**:1410-1414 (May 3) 1924.

28. Wangenstein, O. H.; Leven, N. L., and Manson, M. H.: Acute Pancreatitis (Pancreatic Necrosis): Experimental and Clinical Study, with Special Reference to Significance of Biliary Tract Factor, *Arch. Surg.* **23**:47-73 (July) 1931.

While the experimental evidence and conjectural possibilities offered here may present this method of treatment as a rather perilous one, it must be pointed out that our experimental procedures were not identical with the therapeutic ones advocated by Pribram. For example, we injected the ether into the gallbladder instead of into the choledochus. This probably permitted more ether to remain within the biliary tract. Likewise, our injections of ether were not followed by irrigations with sodium chlorate, which would remove some of the residual ether. Then, too, the amount of ether used in the dogs (from 3 to 6 cc.) was a relatively much larger dose than a similar amount in human beings. We might also mention that we made no effort to prolong the period of survival of the animals by the administration of carbohydrates, a much needed substance in cases of damage to the liver.

While these exceptions may explain the toxicologic toleration of this type of treatment by man, they do not account for Pribram's success in overcoming lithoid obstructions of the choledochus by lavage with ether. Of course, it is entirely possible that all of his cases were those in which the stones were composed of pure cholesterol or at least were not covered with a layer of calcium and were, therefore, readily dissolved by the ether. Then, too, the lavage may have been instrumental in overcoming spasms of the sphincter of Oddi, which may in contracture resist pressures much higher than either the secreting pressure of the liver or the expulsive pressure of the gallbladder.²⁹ A more likely explanation, however, is that the mechanical effects of the injections of ether, sodium chlorate or iodized oil were sufficient to dislodge and remove the cause of the occlusion. Frequent reports of similar experiences have appeared in the literature. For example, about twenty-five years ago Matas³⁰ was "surprised" by the rapid cure of biliary fistulas after catheterization of and injection of fluids into the biliary tract. Neuwirt,³¹ after the injection of 15 cc. of iodized oil into a biliary fistula for visualization, discovered that stones were passed with the stool and via the fistula onto the abdominal wall. More recently, Hicken, Best and Hunt³² summarized their experiences with the statement that "occasionally a lipiodine [iodized oil] lavage of the common

29. Ivy, A. C., and Bergh, G. S.: *Applied Physiology of Extrahepatic Biliary Tract*, J. A. M. A. **103**:1500-1504 (Nov. 17) 1934.

30. Matas, R.: *Catheterization of the Common Duct as a Practical and Effective Upper Route for Enteroclysis Medication in Toxic Biliary Cases (McArthur's Procedure)*, Surg., Gynec. & Obst. **12**:185-186, 1911.

31. Neuwirt, K.: *Therapeutische Wirkung einer Ölfüllung der Gallenwege*, Zentralbl. f. Chir. **57**:1663-1665 (July 5) 1930.

32. Hicken, N. F.; Best, R. R., and Hunt, H. B.: *Cholangiography: Visualization of the Gallbladder and Bile Ducts During and After Operation*, Ann. Surg. **103**:210-229 (Feb.) 1936.

duct will flush out small stones or inspissated plugs of mucus which are causing distress and discomfort in cholecystectomized patients, or perhaps release the sphincterismus."

In conclusion, we can recommend only as thorough as possible surgical removal of the stones in the common duct. If obstruction of the choledochus develops, an injection of the inert iodized oil may be of value not only in visualizing the biliary tract but in the release of the obstruction.

SUMMARY

A closed system for the collection of bile from, and the injection of materials into, the biliary tract is described.

The experimental and theoretical results of direct injection of ether into the biliary tract are discussed.

Attempts to dissolve the usual cholesterol stones in ether are described and dissolved.

Pribram's method is discussed.

CONCLUSIONS

Ether may be very toxic when injected directly into the biliary tract.

The thin layer of calcium so frequently present around a cholesterol stone will prevent the ready solution of the stone by ether.

Lavage of the biliary tract with iodized oil is suggested for removing obstructions of the common duct as well as for visualization.

CARCINOMA OF THE INFRAPAPILLARY PORTION OF THE DUODENUM

MARSHALL M. LIEBER, M.D.

HAROLD L. STEWART, M.D.

AND

HERBERT LUND, M.D.

PHILADELPHIA

The purpose of this communication is to report two new cases of carcinoma of the infrapapillary portion of the duodenum and to review and analyze the previously reported authentic cases of this condition. Of sixty-two cases reported, twenty-eight were regarded as satisfactory,¹ a clinical history and gross and microscopic descriptions of the tumor, obtained at laparotomy or at postmortem examination, being presented in each report. Eight² additional cases, although probably authentic examples of this condition, were not included because the reported data were insufficient for our purposes. Twenty-four cases³ were discarded because the reports lacked a histologic description, and in two others⁴ the exact situation of the tumor was uncertain.

The first reported example of a carcinoma of the infrapapillary portion of the duodenum is usually accredited to Chomel (1852), but the case described by Irwin in 1824 is probably a genuine example of this condition and should take precedence. Since the journal in which this paper was published is not readily accessible, a brief abstract is presented. The patient was extremely emaciated and complained of pain in the epigastrium, which was excruciating at times and was usually

From the Pathological Laboratories of the Jefferson Medical College and Hospital, the Jefferson Hospital Tumor Clinic and the Philadelphia General Hospital.

1. Descroizelle; Baillet; Rolleston; Fenwick; Schieve; Syme; Thaysen; Head; Cade and Devic; Deaver and Ravdin; Vickers; Lundberg; Pommay and Seille; Pauchet and Luquet; Dewis and Morse (cases 7 and 12); Ylvisaker; Schofield; Forni; Meyer and Rosenberg (cases 3 and 4); Mateer and Hartman (case 6); Kellogg; Fariñas Mayo; Sala; Harries and Harrison (case 2); Eger (case 2); Laning and Loy (case 2), and Davis.

2. Larkin; Geiser (case 7); Venot; Markus; Borrmann (case 3); Raiford (cases 44556 and 46153), and Price (case HB 7008).

3. Irwin; Chomel; Williams; Markoe; Whittier (case 13); Herz; Geiser (cases 5, 6 and 8); Bland-Sutton; Erdmann; Crane (case 1); Eusterman, Berkman and Swan (cases 13, 14 and 15); Dewis and Morse (cases 10 and 11); Susman (case 3); Surmont and Tiprez; Rankin and Mayo; Eger (case 2); Lengenmann; Joyce (case 8), and Auvynet.

4. Bandelier (case 6) and Goldberg (case 2).

accompanied by vomiting of a green fluid from two to four hours after meals, obstinate constipation and black feces. About three weeks before death a large tumor was discovered in the right side of the hypochondrium; the prominence was present for from eight to ten days and then subsided. The autopsy report is as follows:

On exposure of the abdominal cavity, the stomach was seen displaced in a singular manner, and enormously distended. This organ occupied almost the whole of the right hypochondrium—its great curvature extending down to the left iliac region. After its removal from the body, it was opened and its contents were found to amount to half a gallon of green bile, somewhat diluted with whiskey and water, which had been taken for common drink. It was then slit from one extremity to the other, carefully washed, and contrary to the opinion I had formed of its condition, not a vestige of disease was to be discovered in any part of this organ. The liver, also, was free from disease, but adherent on its posterior surface—gallbladder much distended with thin green bile. Having examined thus far without being able to detect the seat of the disease, our attention was directed to the duodenum, which was found much enlarged, and externally hard and unyielding. On exposing its cavity, it was found in a cancerous state, and closely studded with tubercles, varying in size from a hickory nut to that of a hazel nut. The largest of them contained matter resembling cream somewhat dried. The whole surface of the seat of ulceration presented a ragged, uneven, lacerated appearance. The quantity of pus found about the diseased part of the gut was upwards of a gill. Pancreas natural in regard to situation, but diminished to one half its usual size and scirrhus. On cutting into it, the interior presented much similarity in colour and texture to that of a boiled cow's udder. Duct natural. . . . The mesenteric glands enlarged—and between the lamina of the mesocolon were contained several tumours of about the size of a large pea, in a state approaching to scirrhus. . . .

The reports of two new cases of carcinoma of the infrapapillary portion of the duodenum follow:

REPORT OF CASES

CASE 1.—R. R., a white man aged 52, was admitted to the Jefferson Hospital on Aug. 28, 1933, with a loss of 30 pounds (13.6 Kg.) in weight and persistent pain in the region of the gallbladder of two months' duration, which suddenly became excruciating two weeks previously. The pain appeared to originate in the right flank posteriorly and radiated along the right costal margin to the area of the gallbladder and occasionally to the region of the right scapula. It was unaffected by the ingestion of fried or fatty foods or sodium bicarbonate. There were associated belching, nausea, vomiting, hiccups and a feeling of fulness and discomfort in the right upper abdominal quadrant. Obstipation developed a week after the acute onset; the urine became dark, and the stools were either black or acholic. Jaundice was first noted by the examining physician. The liver was enlarged and tender, and the abdomen was somewhat distended and rigid on light palpation over the right upper quadrant. When the examiner's thumb was pressed under the right costal margin, the patient would catch his breath on deep inspiration.

Roentgenographic examination of the stomach and intestines was unsatisfactory. No gallbladder shadow was observed after the oral administration of a mixture of tetra-iodophenolphthalein sodium and tartaric acid. The urine contained albumin

and bile pigments but no bile salts. The stools were acholic but later became dark and contained blood and sometimes fat. Repeated drainage of the biliary tract yielded little if any bile. Analysis of the gastric contents after a test meal showed a maximum total acidity of 113 at the end of thirty minutes and a maximum of free hydrochloric acid of 100 at the end of forty-five minutes; lactic acid and bile were absent, and blood was present in all specimens. The Kahn and Wassermann reactions of the blood serum were plus four. The red blood cell count dropped from 4,320,000 on the patient's admission to 2,300,000; the number of platelets increased steadily from 572,000 to 1,055,000. The nonprotein nitrogen content of the blood rose from 38.96 to 90.88 mg. per hundred cubic centimeters of blood; the creatinine content was 1.65 mg., and the cholesterol content, 156 mg. On his admission the reaction to the direct van den Bergh test was positive; the serum bilirubin was 4.2 mg., and 45 per cent of bromsulphalein was retained at the end of thirty minute periods (2 mg. dose). On the day that death occurred the van den Bergh reaction had not changed; the serum bilirubin was 17.45 mg., and 100 per cent of the bromsulphalein was retained. Death occurred on October 3.

Autopsy was performed thirteen hours after death. The combined gross anatomic and microscopic diagnoses were (1) adenocarcinoma of the duodenum, with extension to the pancreas and metastasis to the regional lymph nodes, liver and lungs; (2) hydrohepatosis with marked jaundice; (3) chronic aortitis; (4) arteriosclerosis of the coronary arteries; (5) fatty infiltration of the myocardium, and (6) calcified tuberculous lesions in the lungs.

The posterior wall of the duodenum presented a sharply defined firm round elevated lesion, 3.5 cm. in diameter, which involved the mucous membrane covering slightly more than half the circumference of the intestine. The proximal margin of the lesion occupied a position 13.5 cm. distal to the pylorus and 2.5 cm. beyond the papilla of Vater. The wall of the intestine in the area of involvement was composed of soft gray, homogeneous tissue. This tissue penetrated deeply into the pancreas and more superficially extended beneath the mucous membrane to the margin of the ampulla of Vater. Many of the regional lymph nodes were enlarged and replaced by soft gray, homogeneous tissue adherent to the pancreas and the duodenum. The proximal portion of the duodenum and the stomach and esophagus were markedly distended with fluid and gas. Several small shallow diverticuli were observed on the posterior wall of the duodenum just below the pylorus.

The papilla of Vater was thickened and indurated and appeared more prominent than usual. The ampulla received the duct of Wirsung and the common bile duct, both of which were obstructed. The duct of Santorini opened directly into the duodenum at a point slightly anterior to and 2.5 cm. above the papilla of Vater; it was large and appeared to be continuous with the main pancreatic duct within the body of the pancreas. All the biliary passages were markedly dilated and stained with bile. Obstruction of the biliary tract seemed to result from a combination of neoplastic infiltration of the wall of the ampulla of Vater and from external pressure of the tumor tissue in the duodenum and pancreas and the enlarged lymph nodes in the retroperitoneal space. The wall of the gallbladder was somewhat thickened, and the fundus extended several centimeters below the inferior border of the liver. The liver was enlarged, somewhat cystic and mottled dark green. On section there were innumerable sharply circumscribed gray tumor nodules scattered throughout the parenchyma, the largest of which measured from 4 to 6 cm. in diameter.

Microscopic sections of the duodenum passed through a large tumor nodule, the base of which rested on the muscular coat of the intestine (fig. 1). The epi-

thelial cells extended downward from the mucosal nodule and spread out laterally into the submucosa and in one place penetrated deeply through the muscular wall into the subserous tissue. At the summit of the nodule the duodenal mucosa became atrophic and merged into atypical epithelial cells, loosely distributed and supported by a scant stroma, which formed the core of several tall, villus-like structures. The blood vessels of the stroma were often thin and immature. The atypical epithelial cells were round, oval or polyhedral, with smooth acidophilic or pale foamy cytoplasm. The nuclei were hyperchromatic or pale, vesicular, small or large, often crescentic, lobulated and eccentrically placed in the cell. As a rule they were single, but many individual cells contained from two to ten nuclei. There were a few bluish interlacing strands among these epithelial cells, suggesting



Fig. 1.—Microscopic section of the duodenum at the margin of the tumor, showing infiltration and destruction of all the coats of the intestine; circa $\times 7$.

the presence of mucin. Scattered through the nodule were a number of polymorphonuclear leukocytes, usually in association with necrotic areas, which were numerous in the sections. There were many collections of round cells and a few polymorphonuclear leukocytes in the deeper layers of the musculature. The metastatic lesions in the lung and liver resembled the primary nodule in the duodenum. There were several large neoplastic nodules lying in relation to some of the ducts in the pancreas, which showed a moderate degree of fibrosis about the smaller ducts. In this situation, as in the metastatic lesions of several of the lymph nodes, the atypical epithelial cells were paler; they tended to form better developed acini and contained more mucin than the primary duodenal nodule. Several areas of tumor tissue were observed in and about small thin-walled vessels outside the capsules of some of the lymph nodes.

The hepatic parenchyma presented the characteristic picture of biliary stasis, with necrosis and pigmentation about the central veins, proliferation of the smaller bile ducts, marked peribubular fibrosis and round cell infiltration and a few lesions of biliary necrosis.

CASE 2.—P. S., a Negress aged 51, under treatment for diabetes and hypertension of at least a year's duration, was admitted to the Philadelphia General Hospital on Oct. 23, 1933, with nausea, vomiting, abdominal pain, diarrhea and constipation. The onset occurred suddenly ten days previously, with steady epigastric pain, which became worse on eating, and diarrhea. This was succeeded by obstinate constipation and vomiting of clear liquid and recently ingested food. On physical examination the skin was dry, and the breath smelled of acetone. Three liters of foul-smelling fluid was siphoned off through a stomach tube. Roentgenographic examination of the gastro-intestinal tract after the ingestion of a barium sulfate meal disclosed a dilated, atonic stomach, which had a persistent filling defect on the greater curvature of the pylorus. The duodenal cap was well outlined and seemed perfect, but beyond this point little barium sulfate was observed to pass, which gave a slightly granular appearance to the remainder of the duodenum. The lower portion of the intestinal canal seemed normal after a barium enema. There was no anemia; the chloride content of the blood was 584 mg. per hundred cubic centimeters; the sugar content varied between 130 and 234 mg., and the Kahn reaction of the blood serum was negative. The urine contained a faint trace of albumin and had a specific gravity of from 1.015 to 1.039.

At laparotomy, on November 11, a firm nodular constriction was found which was thought to be a tumor of the pylorus, and gastro-enterostomy was performed for relief of obstruction. On the sixth postoperative day a suppurative lesion developed in the right parotid gland, which was incised and drained on November 20. A sinus tract formed and later ruptured into the right external auditory canal, resulting in paralysis of the right side of the face. The patient died on December 9 from an infection of the blood stream.

Autopsy was performed nine hours after death. The combined gross anatomic and histologic diagnoses were: (1) adenocarcinoma of the infrapapillary portion of the duodenum, with extension to the pancreas and metastasis to the liver; (2) marked dilatation of the proximal portion of the duodenum; (3) a patent gastro-enterostomy opening; (4) abscesses of the right parotid gland and kidney; (5) arteriosclerosis of the aorta and the renal, coronary and pancreaticoduodenal arteries; (6) acute degeneration of the myocardium and renal tubular epithelium; (7) congestion of the lungs, spleen and liver; (8) interstitial fibrosis of the pancreas, and (9) fatty change of the liver.

About 11 cm. from the pylorus the duodenum presented an annular constriction 3 cm. in diameter, with a lumen which barely permitted the passage of a fine probe. The wall of the duodenum at the point of involvement was composed of firm white tissue, which infiltrated the head of the pancreas. The proximal portion of the duodenum was markedly dilated. The common bile duct was patent, slightly thickened and measured 1.5 cm. in diameter; bile could be expressed through the ampulla of Vater, which lay 1 cm. proximal to the duodenal lesion. No metastatic nodules were observed in the abdominal lymph nodes.

Microscopic sections through the lesion included the duodenum and an adjacent portion of the pancreas (fig. 2). The strip of mucous membrane terminated abruptly at either end and did not show a transition laterally into malignant tissue. In the deeper layers of the mucosa and muscularis mucosa were several nodules of atypical cells with pink cytoplasm and hyperchromatic nuclei, frequently with large

multiple lobulations and numerous mitotic figures. The cells around the periphery of these nodules tended to form columnar rows resembling the cells in the depths of the duodenal crypts. The entire submucosa was invaded by nests and strands of tall columnar vacuolated cells, which occasionally formed elongated acini and closely packed cellular nests. They penetrated through the muscular coats into the septums of the pancreas for a short distance. The stroma was moderate in amount and infiltrated with small round cells.

The liver showed metastatic lesions, acute congestion, central lobular cytoplasmic vacuolation and a moderate degree of periportal round cell infiltration. The kidney was intensely congested and contained a focus of early suppuration in the medulla.

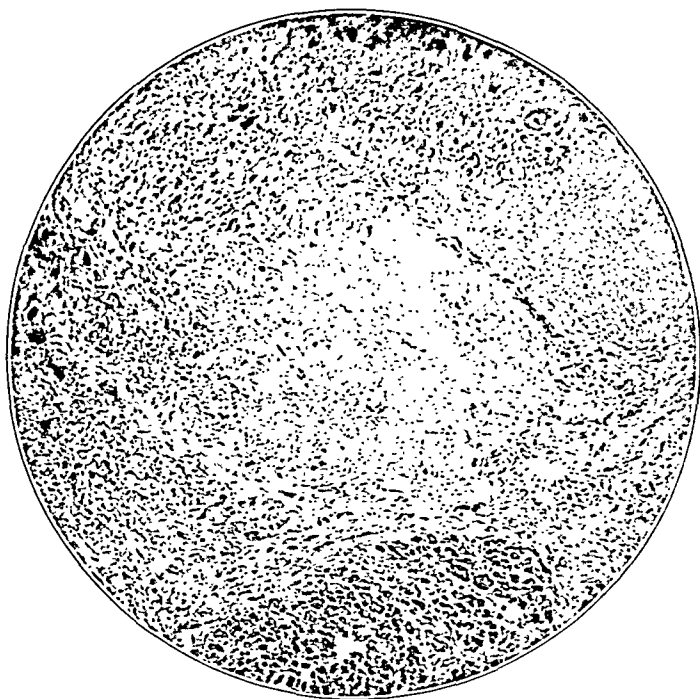


Fig. 2.—Microscopic section of the wall of the duodenum just beneath the ulcerated area. There were atypical epithelial cells in the submucosa, which permeated through the muscular coats into the septums of a small portion of the pancreas attached to the deeper portion of the section; $\times 40$.

AGE AND SEX; INCIDENCE

In the series of cases studied the patients consisted of twenty men ranging in age from 40 to 74 years, with an average age of 58.2 years, and ten women (two Negresses) ranging in age from 35 to 61 years, with an average age of 48.3 years.

Carcinoma arising in the duodenum is estimated to be found in from 0.01 to 0.1 per cent of all postmortem examinations. The per-

centages commonly given range from 0.01 to 0.03 (Eusterman and Balfour). Nearly one half of the malignant growths of the small intestine are said to develop in the duodenum (Kellogg), but these statistics are based on reports in the literature, and many of these are not authentic cases. Of the two new cases here reported, one was found at the Jefferson Medical College Hospital in a series of 3,526 autopsies and the other at the Philadelphia General Hospital in a series of 20,176 autopsies performed since 1920.

ANATOMY

Textbooks on anatomy usually state that the duodenum is divided into the following parts: (1) the superior portion, from 3 to 5 cm. in length, which commences at the pylorus and passes upward and backward, where it forms, with the second portion, the superior flexure; (2) the descending or vertical portion, from 8 to 12 cm. in length, which receives the bile and pancreatic ducts and forms with the third portion the inferior flexure; (3) the inferior portion, which is again subdivided into (*a*) the horizontal portion, from 8.5 to 10 cm. in length, which terminates in (*b*) the ascending portion, from 3 to 7 cm. in length, this in turn terminating in the duodenojejunal flexure.

Any division of the duodenum which fails to take into consideration the point of entrance of the bile and pancreatic ducts is inadequate for clinical purposes. Embryologically, all of the duodenum above the papilla of Vater is developed from the foregut, and the remainder of the small intestine is derived from the yolk sac, or so-called midgut. With the papilla of Vater as an orientating mark for subdivision, that portion of the duodenum above is the suprapapillary segment; that below, the infrapapillary segment.

The infrapapillary portion extends from the papilla of Vater to the duodenojejunal junction. It consists of three subdivisions, which are best seen in the U-shaped duodenum, less well in the C-shaped type and not at all in the V form: 1. The descending portions extend along the right side of the vertebral column from the papilla of Vater to the inferior angle on a level with the upper border of the body of the fourth lumbar vertebra. It is in relation in front with the transverse colon and small intestine and behind with the right kidney in the neighborhood of the hilus, the renal vessels, the inferior vena cava and the psoas muscle. At its medial side are the head of the pancreas and the common bile duct and laterally the right colic flexure. 2. The horizontal portion, from 5 to 7.5 cm. long, begins at the inferior angle, passes from right to left, with a slight inclination upward in front of the great vessels and crura of the diaphragm, and ends in the ascending portion in front of the aorta. It is crossed by the superior mesenteric vessels and the mesentery. Its posterior surface lies on the right crus

of the diaphragm, the inferior vena cava and the aorta, and the upper surface is in relation with the head of the pancreas. 3. The ascending portion, 2.5 cm. long, extends along the left side of the aorta as far upward as the level of the superior border of the second lumbar vertebra, where it turns abruptly forward to end in the duodenojejunal flexure. It lies in front of the left psoas muscle and left renal vessels.

MORBID ANATOMY

The dimensions of the primary tumor in the duodenum were stated in twenty-five cases. In a little over half of these it measured from 3 to 5 cm. in length, in six cases from 1 to 2.5 cm. and in five cases from 6 to 8 cm. In Rolleston's case the infrapapillary segment was involved in its entirety. A circumscribed tumor 4 cm. or less in diameter was localized just beyond the papilla of Vater in eight cases and at or near the duodenojejunal flexure in thirteen. In eight cases the proximal margin of the growth was situated near the papilla of Vater, and the distal margin of the neoplasm did not extend beyond the horizontal portion of the duodenum, except in the extensive growth considered previously. Ulceration was present in sixteen cases. A few ulcers were crater-like, measuring upward of 6 cm. in diameter, with margins variously described as hard, resistant, cicatrized, indurated, friable, rolled or elevated. A gaping artery was present in the floor of one ulcer, and perforation occurred in four.

The primary tumor was completely annular in nineteen cases and was confined to the posterior or the median wall or to both in six. Some degree of stenosis was present in all cases, being complete or almost complete in seventeen. The annular tumors were frequently fixed and consisted of compact grayish white cicatricial-like tissue. The non-annular growths were polypoid or pedunculated and usually soft in consistency.

Proximal to the primary duodenal lesion, the alimentary canal was regularly dilated well up into the esophagus. The proximal portion of the duodenum was frequently distended in a funnel-shaped or pyriform manner, and its mucous membrane was flattened and atrophied or occasionally puckered and thrown into folds, while the muscular coats were usually attenuated but occasionally were thick and hypertrophied. The pyloric sphincter showed marked thinning, and the orifice was dilated, sometimes to a diameter of 12 cm., the stomach and duodenum together often appearing as a bilocular viscus. The gastric contents occasionally measured 1,500 cc. and consisted of degenerated blood and remnants of food. In Schiewe's case the stomach was the size of a "pig's bladder," with the pylorus in the right anterior axillary line and the duodenum the width of a normal colon. Fenwick stated that the

anterior abdominal cavity of his subject was chiefly occupied by two thin-walled sacs lying side by side; the one on the left consisted of a dilated stomach, while the other, which was ovoid and 8 inches (20 cm.) in length with a maximum circumference of 13 inches (33 cm.), represented the upper two thirds of the duodenum. In occasional cases in which the clinical manifestations indicate low grade, long-continued obstruction, the wall of the stomach and proximal portion of the duodenum may become markedly hypertrophied. Rolleston explained this change on the basis that from time to time food collects proximal to the obstruction and, by forcing the duodenum downward, leads to complete closure of this fixed and already strictured portion of the bowel.

Metastases or extension of the primary tumor to adjacent structures occurred in fifteen cases. Metastatic deposits were present in the lymph nodes in ten, in the liver in seven and in the lungs in two. The regional nodes were involved in all ten cases of lymphatic metastases, the mesenteric nodes in four, the retroperitoneal nodes in three and the periportal nodes in three, while in one case practically all the visible nodes in the abdomen and pelvis were affected. Adhesions to the surrounding structures were encountered in half the cases, but which of these were neoplastic could not be accurately estimated. Neoplastic extensions into the pancreas occurred in five cases, and into the surrounding fat, posterior abdominal wall and aorta, in one each. The largest tumorous deposits in the pancreas did not exceed 3 cm. in diameter. The primary and infiltrating tumors together with the cancerous lymph nodes and adhesions sometimes produced a large fixed neoplastic mass, which compressed surrounding tissues and viscera. Obstruction of the terminal end of the common bile duct or the ampulla of Vater occurred in five cases, due in most instances to extension of the primary neoplasm.

Perforation of the duodenum occurred in four cases. Rupture developed spontaneously in Dewis and Morse's case 12, and the resulting lesion was walled off by surrounding tissues. In Pommay and Seille's case, fistulous formation occurred three days after gastroenterostomy and biopsy and resulted in diffuse peritonitis. In Schofield's case perforation occurred after the implantation of radon seeds, which were believed to have interfered with healing of the duodenostomy wound. Perforation in Ylvisaker's case was found fifteen days after incision and drainage of the pancreas and several months after high voltage roentgen therapy over the epigastric region.

Morbid anatomic lesions other than the foregoing were mentioned only rarely. Chronic pancreatitis was observed in six cases, suppurative pancreatitis in one and obstruction of the duct in Wirsung in two. Of five cases in which biliary stasis was present, the hepatic changes

were described in one and resembled those resulting from biliary obstruction due to other causes. Chronic cholecystitis was found in two cases, suppurative cholangitis in one, pyemia in two and biliary calculi in one. Degenerative changes in the tubular epithelium of the kidney were frequently noted. Inflammatory hyperplasia of the lymph nodes in the upper part of the abdomen was regularly associated with extensive infection in and about the primary duodenal neoplasm.

HISTOLOGIC PICTURE

The lesion was designated as a glandular carcinoma in all cases, but aside from this statement microscopic data were scanty. Biopsy material or the entire surgical specimen was obtained for examination by laparotomy in nine cases. The growth was of the scirrhus type in seven cases, the medullary type in four and the mixed scirrhus and medullary type in two. Papillary formations were marked in five cases, and variable amounts of mucin were present in four; in two of these the formation was described as a mucinous adenocarcinoma. Variations from a well differentiated carcinoma of the intestinal type with cylindric cells to one of rather marked anaplasia were described, and in ten cases anaplasia and rapid cellular division were noted. Inflammatory changes were regularly present in the connective tissue stroma and were pronounced in three cases in which ulceration was present.

PATHOLOGIC PHYSIOLOGY

There are relatively few studies of the abnormal physiologic changes associated with clinical obstruction of the infrapapillary segment of the duodenum. In animals, Elman and Hartman concluded that the principal cause of death is a change in the chemical constituents of the blood, resulting primarily from the loss of gastro-intestinal secretions and secondarily from circulatory and renal insufficiency due to dehydration. By introducing a solution of sodium chloride below the point of obstruction, life can be maintained in experimental animals, whereas the reintroduction of bile and pancreatic juices fails (Armour, Brown, Dunlop, Mitchell, Searls and Stewart). Owing to the similarity between the toxic reaction of the material from obstructed loops of bowel and that of histamine, Dragstedt suggested that the latter was formed by the bacterial decomposition of histidine as the result of stasis. He expressed the belief that histamine accelerates the secretogogic action of the intestines and that the excessive secretion in turn facilitates distention and consequent breakdown of the normal resistance of the intestinal mucosa against toxic material in the lumen of the bowel. It is also probable that death is hastened by slow absorption of histamine-like

substances, which are believed to accelerate chemical changes occurring as a result of loss of gastric secretion (Andrus, Guest, Gates and Ashley).

From a clinical point of view the signs and symptoms of obstruction of the type considered in this paper have been divided by Rivers and Thiessen into two groups. In the first are included symptoms arising from local mechanical disturbances or those incident to neoplastic invasion of surrounding tissues. The second group includes systemic disturbances arising as a part of the toxemia associated with obstruction together with the manifestations of malignant cachexia, metastasis and extension. On the basis of previous studies it has been shown that the symptoms resulting from interference with normal peristalsis are flatulence, nausea and regurgitation of food, which may not reach their maximal intensity for an hour or more after eating. Vomiting of the retention type develops, even with incomplete obstruction, and leads to varying degrees of malnutrition and dehydration. At first the stenosis is adequately counteracted by increased peristalsis, but later compensation becomes inadequate, and signs and symptoms of partial or complete obstruction may supervene rapidly. Obstruction by malignant disease is rarely intermittent, and relief is seldom obtained except by surgical measures. Since the lesion is situated below the ampulla of Vater, the vomitus or gastric contents obtained by lavage usually contain bile in liberal amounts, except in occasional instances in which the biliary passages as well as the intestine are obstructed.

CLINICAL FEATURES

Onset.—The onset of the condition was acute in twelve cases, gradual throughout in twelve and first gradual and then acute in six. A history of antecedent illness was elicited in three cases in which the onset was acute and in seven cases in which the course was gradual throughout.

The duration of the condition in eleven cases in which the onset was acute ranged from fourteen days to seven months, averaging slightly less than four months. In one case the patient was not traced after operation and discharge from the hospital. The initial symptoms in this group consisted of epigastric distress or pain (twelve cases), vomiting (ten), loss of weight and strength and anorexia (five), a sense of abdominal weight or pressure (two), belching (two) and constipation, diarrhea, abdominal distention, hiccups and bulimia (one each). Later manifestations included constipation (four), loss of weight and strength and anorexia (four), and jaundice, vomiting, a sense of weight or pressure in the abdomen and abdominal distention (one each).

The duration of the condition in cases in which the course was gradual throughout ranged from five to nineteen months, averaging slightly less than eleven months in nine instances; the ultimate fate of three patients was not stated. Initial symptoms in this group consisted of pain (six cases), vomiting (five), loss of weight and strength (two), abdominal distention (two) and a sense of weight or pressure in the abdomen, belching and diarrhea (one each). Later manifestations were loss of strength and weight and anorexia (eight cases), pain (four), vomiting (four), diarrhea (three), abdominal distention (two) and a sense of weight or pressure in the abdomen and constipation (one each).

In the group in which the course was at first gradual and then acute, the duration of the first stage was approximately ten months and of the second, approximately four and a half months, the average total duration being about eleven months. The gradually developing symptoms included pain (three cases), a sense of weight or abdominal pressure (one) and loss of weight and strength (one). The subsequent acute manifestations were vomiting (five cases) and flatulence, jaundice, abdominal distention, constipation and loss of weight and strength (one each). Still later, there were loss of weight and strength and anorexia (two cases), constipation (two) and pain, jaundice and abdominal distention (one each).

The clinical diagnoses in the cases in which there was an antecedent history were reported as lead poisoning, cholecystitis, neurosyphilis, traumatic rupture of the intestine and arteriosclerosis with diabetes and with hypertension (one case each) and simple ulcer (two). In the remaining three cases the patients complained of symptoms referable to the upper part of the abdomen which were not diagnosed.

Pain.—Pain was present in all but one case and was usually severe and sometimes colicky or cramplike. It was frequently intermittent at first, then increased markedly in severity and eventually became continuous. In a few cases there was simply epigastric distress, slight burning or a feeling of distention and fulness. Pain occurred with the onset in twenty-two cases and later in seven. It was situated in the epigastrium in twenty-one cases, in the right upper abdominal quadrant in three, in the lower part of the abdomen in two and in the right flank posteriorly in one. Radiation to the back occurred in four cases and to the region of the shoulders in two. This symptom occurred from one half to two hours after meals or was aggravated or intensified by food in seventeen cases, while in three cases it was unaffected by food. Relief sometimes followed the ingestion of food, vomiting or lying on the right side, and in one case both pain and meteorism disappeared after the administration of morphine. Attacks of severe pain were

sometimes followed by epigastric burning, discomfort and a sense of weight in the abdomen and in one case these were preceded by hunger and followed by vomiting. There was associated tenderness in eight cases and abdominal rigidity in two.

Vomiting.—Vomiting was present in twenty-five cases, absent in four and not mentioned in one. It appeared with the onset in seventeen and after the onset in eight, usually occurring from a few minutes to several hours after meals. It was at first intermittent and tended to become incessant terminally and was only occasionally associated with nausea. The vomitus was frankly bilious in ten cases, and in three contained coffee-ground material; sometimes food ingested from several hours to several days previously was present, in which case the vomitus often had a foul odor due to putrefactive changes. Some patients had gastric succorhea, and the amount of fluid vomited exceeded that ingested; in Rolleston's case 11 pints (6.2 liters) was vomited in fifteen hours, and in Fenwick's case 13 ounces (0.4 liter) of bilious fluid was obtained from the stomach, which had been emptied and without food since the previous night. Vomiting occurred at any time of the day or night and was not associated with any particular kind of food. Sometimes, however, the patients vomited at regular intervals, as, for example, after meals, once a day or periodically every second day. Of the four cases in which vomiting was absent (Deaver and Ravdin; Pommay and Seille; Pauchet and Luquet, and Ylvisaker), the primary lesion was ulcerated in all, markedly obstructive in only one, perforated in two, annular in two and fungating in one, and there was dilatation of the proximal duodenal segment in three. Similar anatomic conditions were present in other cases in which vomiting was a marked symptom.

The vomitus or material removed for gastric analysis in twenty cases revealed the presence of bile in fourteen and blood in seven. The absence of bile from the vomitus in two cases can be attributed to the development of complete biliary obstruction. Free hydrochloric acid was absent in eight of fourteen specimens, and in one of these the reaction was alkaline. In the remaining six specimens the free hydrochloric acid varied from 5 to 100. The total acidity varied from 9 to 100 in nine specimens; being above 40 in 6. In Laning and Loy's case, in which the gastric contents were analyzed after the injection of histamine, the free hydrochloric acid and total acidity were unaffected in all specimens.

Jaundice.—Jaundice developed in three cases relatively late in the course. In Schofield's case the proximal margin of the growth encroached on the ampulla of Vater. In Meyer and Rosenberg's case 3 the primary tumor consisted of a large constricting mass just below the papilla of Vater, and there was marked dilatation of the biliary and pancreatic

ducts and suppurative cholangitis. In our case 1 the proximal margin of the tumor was 2.5 cm. distal to the papilla of Vater and had extended proximally beneath the mucosa into the wall of the ampulla; the bile and the pancreatic ducts were further compressed by masses of tumor tissue in the duodenum, pancreas and retroperitoneal lymph nodes. The late development of jaundice is consistent with the observations made at autopsy in that obstruction to the extrahepatic biliary passages occurs relatively late from extension and metastasis to the pancreas, surrounding tissues and regional lymph nodes and exceptionally, in part, from the pressure of a large primary cancer. Of interest in this connection is the statement by Rivers and Thiessen that the appearance of icterus with obstructive lesions of the infrapapillary portion of the duodenum is an almost certain indication of malignancy.

Morbid conditions tending to cause biliary obstruction and jaundice were present in incipient form in several other cases. In Rolleston's case the tumor had reached the biliary papilla, and the common bile duct was dilated as a result of beginning obstruction. In Schiewe's case, although the papilla of Vater was encircled by neoplastic tissue, there was no apparent biliary obstruction and no jaundice. Similarly, in Dewis and Morse's case 7 and in our case 2 the common bile duct was slightly dilated, but jaundice was not yet apparent. Gallstones played no part in the production of jaundice, being present in only one instance and then in the gallbladder. Of the five cases in which there was partial or complete biliary obstruction, bile was detected in the gastric contents in two, was absent in one and was not mentioned in two.

Constipation and Diarrhea.—Constipation or obstipation was reported in nine cases, occasionally in association with roentgenographic evidence of stasis in the colon. Diarrhea occurred in five cases, as a transitory manifestation at the onset in two and in association with lead poisoning in another. So-called pancreatic diarrhea was reported only once. The stools of one patient were acholic, while those of two others, with bilious vomiting and tight strictures of the infrapapillary portion of the duodenum, contained bile. One patient with jaundice had stools which were dark because of the presence of blood.

Other Laboratory Data.—Patients with carcinoma of the infrapapillary portion of the duodenum tend to have marked anemia and slight leukocytosis, especially during the cachectic phase. Of nine cases in which it was possible to estimate the color index, it was high (from 0.9 to 1.1). An abrupt decrease in red blood cells was a terminal feature associated with loss of blood in the vomitus and stools. Evidences of impairment of hepatic and renal function were present in our case, with obstructive jaundice. Marked nitrogen retention occurred in one case, with incessant vomiting, nephrosis and an extreme degree of

duodenal obstruction. The results of urinalysis were reported in eighteen cases; in ten the urine was said to be normal; albumin was present in six, bile in three, indican in one and diminished amounts of chlorides and increased quantities of creatine in one.

Roentgenographic Studies.—Roentgenograms of the gastro-intestinal tract were taken after a barium meal in eighteen cases; in three the studies were unsatisfactory. In the others the findings were so varied that a brief analysis of each case seems warranted.

There were six cases in which the lesion was fairly well localized. In Pauchet and Luquet's case the barium did not pass beyond the fourth segment of the duodenum, the third portion being markedly dilated and having the appearance of the stomach. Anatomically, there was an ulcerated constricting lesion near the duodenojejunal junction. In Mateer and Hartman's case there were a filling defect in the third portion of the duodenum and stasis of barium in the proximal segments and stomach; at autopsy a large ulcerated lesion was found 4 cm. below the papilla of Vater. In Farinas Mayo's cases there were ptosis and distention of the stomach and dilatation of the duodenum up to its junction with the jejunum. Fluoroscopic examination showed active peristaltic and antiperistaltic movements, the barium being carried to the duodenojejunal angle; at the end of six hours almost the entire barium meal was still retained in the duodenum, which was maximally distended. Anatomically, there was a completely stenotic annular lesion at the duodenojejunal angle. In Lundberg's case the wide open pylorus was recognized, and the duodenum was well filled and very wide in its lower portion; strong peristalsis and successive contractions of the circular muscles were seen here, and the lumen was still filled after four hours. Autopsy disclosed a completely annular lesion at the duodenojejunal junction. In Sala's case there were dilatation and stasis of the duodenal cap and stasis and deformity of the descending portion of the duodenum, which was interpreted as being due to external pressure by a pancreatic tumor. Autopsy revealed an ulcer of the infra-papillary portion 5 cm. in diameter, extensive local adhesions and masses of cancerous lymph nodes; the pancreas, however, appeared to be normal. In Kellogg's case the gastric retention noted clinically was attributed roentgenographically to adhesions involving the second and the fourth duodenal segment; at autopsy an almost totally obstructive lesion was found near the terminal end of the duodenum.

There were five cases in which the roentgenographic picture suggested the presence of a lesion at or near the pylorus. In Deaver and Ravdin's case a roentgenographic diagnosis was made of adhesions or ulcer near the pylorus, the duodenum being reported as probably normal; at autopsy an ulcerated tumor was situated below the papilla of Vater.

In Vicker's case the column of barium was obstructed just beyond the pylorus, the stomach being huge and atonic; at laparotomy the tumor was found in the region of the duodenojejunal flexure. In Forni's case the duodenal bulb was partially filled with barium, but there was none in the remainder of the duodenum; at autopsy an annular almost totally obstructive lesion the size of a hen's egg was found in the third portion of the duodenum. In Harries and Harrison's case a filling defect of the pylorus was observed, with marked dilatation of the stomach, and a diagnosis of carcinoma of the pylorus was made; at laparotomy the neoplasm was found at the duodenojejunal flexure. In our second case a filling defect was observed at the pylorus, and at autopsy an annular stenosing cancer was found 11 cm. beyond the pyloric ring.

No suggestion of a lesion was observed roentgenographically in four cases, even though the morbid anatomic changes were striking. In Meyer and Rosenberg's case 3 there was marked obstruction by a fungoid mass, 5 by 6.5 cm., just below the papilla of Vater. In Davis' case there was a practically annular lesion, measuring 3.3 cm. in diameter, near the terminal end of the duodenum. In Laning and Loy's case the third portion of the duodenum was practically completely stenosed by an ulcerating mass 5 cm. long. The roentgenographic examination in Head's case was made seven months before death, and at autopsy the lumen of the intestine was almost completely occluded by a large cauliflower-like growth.

From an analysis of these data it is apparent that the accuracy of roentgenographic diagnosis in six cases is somewhat offset by the fact that in five the lesion was localized incorrectly at or near the pylorus and in four others no lesion could be demonstrated.

PHYSICAL EXAMINATION

A mass was palpated in the region of the primary tumor in five patients, and a doubtful or suggestive mass was felt in two. The mass was movable in three cases, moved with the respirations in one and was associated with tenderness in three and with rigidity in one. Tenderness was elicited in six other cases in which masses were not palpable, in two of which there was associated abdominal rigidity. In Schiewe's case marked pulsations were transmitted through a palpable tumor mass, which at autopsy was found to be adherent to a locally stenotic aorta. The presence or absence of a palpable mass was correlated with the size of the local tumor together with the associated inflammatory and neoplastic lesions; it was found that many large anatomic specimens were not detected during life, yet in one case an exceedingly small primary tumor was palpated. Conditions other than the primary tumor

were occasionally noted on palpation. For example, palpation of the liver and gallbladder gave evidence of biliary stasis, and metastatic lesions on the liver and in the deep and superficial lymph nodes were noted. Dilatation of the stomach, sometimes to the iliac crest, was noted in eight cases, often with visible peristalsis and a succussion splash, which Fenwick heard below the navel and laterally in the anterior axillary line.

DIAGNOSIS

The diagnosis of carcinoma of the stomach was made in ten cases, in six of which the growth was believed to involve the pyloric region. In twelve cases the following diagnoses were made: carcinoma of the small intestine, obstruction of the small intestine, pyloric obstruction, pyloric stenosis from ulcer, retroperitoneal tumor, carcinoma of the head of the pancreas, duodenal or jejunal stenosis, duodenal ulcer with carcinoma superimposed and organic obstruction at the duodenojejunal flexure.

A correct diagnosis was made at laparotomy in thirteen of twenty-one cases, and in three no diagnosis was recorded. The diagnoses made in five cases were: carcinoma of the small intestine, a mass of doubtful nature in the third portion of the duodenum, hypertrophy of the pyloric sphincter, retroperitoneal sarcoma and carcinoma of the pylorus. One patient was twice subjected to laparotomy, and a mistaken diagnosis of hypertrophied pylorus was made on each occasion.

TREATMENT

The treatment of carcinoma of the *infrapapillary* portion of the duodenum has been either symptomatic or palliative or directed toward cure. Rational therapy for definitely obstructive lesions has been outlined by Rivers and Thiessen with a view of combating the toxemia in preparation for operation. Radiation therapy was employed in two cases (Ylvisaker and Schofield). Laparotomy was performed in twenty-one cases, and the procedures and results are presented in the accompanying table. The results were unsatisfactory in seventeen cases, and the ultimate fate of the patients in the remaining four cases was not determined, two of them being alive three months after operation, one of whom had extensive metastases. Schofield's case is of particular interest in view of his original method of treatment. First he performed biopsy, cholecystoduodenostomy and posterior gastro-enterostomy and six weeks later reopened the duodenum and implanted radon seeds directly into the tumor. A duodenal fistula developed, and the patient died on the twenty-ninth postoperative day, but no evidence of neoplastic tissue could be detected at this time, the tumor evidently being quite radiosensitive.

A review of the morbid anatomic data in the present series of cases indicates the difficulties which may be encountered in carrying out surgical treatment. There was extension or metastasis or both in fifteen cases—in ten to regional lymph nodes, in five to the pancreas, in one

Results of Operation in Twenty-One Cases of Carcinoma of the Infrapapillary Portion of the Duodenum

Date	Authors	Operative Procedures	Period of Survival	Cause of Death
1904	Syme	Resection and end to end anastomosis	Alive 3 mo. later	
1917	Thaysen	Gastro-enterostomy	Died several days later	Hemorrhage
1919	Cade and Devic	Gastro-enterostomy	Died 36 hr. later	
1920	Deaver and Rardin	Gastro-enterostomy	Died 2 hr. later	Shock
1924	Vickers	Gastro-enterostomy	Died 2 mo. later	
1924	Lundberg	Sept. ?; operation for traumatic rupture of intestine; Nov. 4: resection and end to end anastomosis	Alive 3 mo. later	
1925	Pommay and Seille	Gastro-enterostomy	Died 4 days later	Perforation and peritonitis
1927	Pauchet and Luquet	Resection		
1928	Dewis and Morse (case 7)	March 26: gastro-enterostomy; April 9: relief of obstruction due to kinking of bowel	Died 2 days later	
1929	Ylvisaker	Incision and drainage of pancreas	Died 15 days later	Hemorrhage
1930	Kellogg	Gastro-enterostomy	Died 8 days later	
1930	Schofield	April 16: cholecystoduodenostomy and gastro-enterostomy; May 28: radon seeds implanted	Died 29 days later	
1931	Meyer and Rosenberg (case 4)	Gastro-enterostomy and surgical ligation of duodenum	Died several weeks later	
1931	Forni	July 1930: exploratory; July 1931: gastro-enterostomy	Died about 3 mo. later	
1932	Mateer and Hartman	April: cholecystostomy; July: exploratory	Died 12 days later	Hemorrhage and shock
1934	Farinas Mayo	Resection		
1935	Davis	Resection and end to end anastomosis	Died 7 days later	
1935	Harries and Harrison	Resection and end to end anastomosis	Died 3 mo. later	
1935	Laning and Loy	March 15: cholecystostomy; March 25: gastro-enterostomy	Died 11 days later	Myocardial failure
1935	Sala	Exploratory	Died 5 days later	
1936	Author's case 2	Nov. 11: gastro-enterostomy; Nov. 17: incision of parotid abscess	Died 3 days later	Suppurative parotitis and pyemia

each to the posterior abdominal wall, surrounding fat and aorta and in approximately five to the ampulla of Vater and the common bile duct. Since these figures are based on routine autopsy, biopsy and surgical examination, it is probable that the true incidence of extension and

metastasis is much higher. Obviously all these factors must be taken into consideration in determining the therapeutic measures to be employed in individual cases.

SUMMARY AND CONCLUSIONS

A clinical and pathologic study is presented of thirty cases of carcinoma of the infrapapillary portion of the duodenum—two new cases and twenty-eight selected from the literature.

One of the new cases was found in 3,526 autopsies and the other in 20,176 autopsies.

Sixty-six per cent of the patients were men and 33 per cent were women; the average age was 58.2 years for the men and 48.3 years for the women.

The clinical onset was acute in 40 per cent of cases, with an average duration of four months; it was gradual throughout in 40 per cent, with an average duration of eleven months, and first gradual and then acute in 20 per cent, with an average duration of ten months, the gradual phase occupying four and a half months. The principal symptoms and signs irrespective of the mode of onset were pain, vomiting and cachexia. Other less common symptoms included anorexia, constipation, diarrhea, abdominal distention and jaundice. The vomitus or gastric contents were analyzed in twenty cases, and bile was detected in 70 per cent of these and blood in 35 per cent; free hydrochloric acid was absent in 57 per cent of fourteen specimens. A mass in the region of the primary tumor was palpated clinically in 16.6 per cent of the cases.

A correct preoperative clinical diagnosis is rarely made. An obstructing lesion of the duodenum was visualized roentgenographically with a fair degree of accuracy in 40 per cent of fifteen cases; in 33 per cent the lesion was incorrectly localized at or near the pylorus, and in the remainder no lesion was demonstrated. A correct diagnosis was made at laparotomy in 61.9 per cent of twenty-one cases, the results being unsatisfactory in 81 per cent of these, and the postoperative follow-up studies were incomplete in the remainder.

The primary tumor measured from 3 to 5 cm. in length in the majority of cases, and in one case the infrapapillary segment of the duodenum was involved diffusely in its entirety. All the tumors were of the glandular carcinomatous variety. The descending and ascending portions of the infrapapillary segment were most frequently involved. Extension of the primary tumor to adjacent structures and organs and metastases or both occurred in 50 per cent of cases. Some degree of obstruction of the terminal end of the common bile duct or of the ampulla of Vater or both occurred as a terminal feature in 16.6 per cent. Duodenal fistulas existed in 13.3 per cent. A high grade of

intestinal obstruction was present in 56.6 per cent. The alimentary canal proximal to the primary duodenal lesion was maximally distended, the stomach and proximal portion of the duodenum often giving the appearance of a bilocular viscus.

In dealing with duodenal cancer clinically or pathologically, the papilla of Vater is the most important anatomic landmark in this region.

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EXPERIMENTAL PEPTIC ULCER PRODUCED BY CINCHOPHEN

METHODS OF PRODUCTION, THE EFFECT OF A MECHANICAL IRRITANT
AND THE LIFE HISTORY OF THE ULCER

LEONARD K. STALKER, M.D.

Fellow in Surgery

JESSE L. BOLLMAN, M.D.

AND

FRANK C. MANN, M.D.*

ROCHESTER, MINN.

Cinchophen has been used since 1911 in the treatment of gout. Toxic cirrhosis of the liver has developed in a few cases after its use. In attempting to produce hepatic damage experimentally in dogs, Churchill and Van Wagoner¹ in 1931 noted peptic ulcer in many of their animals. This and subsequent work by these investigators suggested to us that we attempt to produce peptic ulcer by the administration of cinchophen. Ulceration developed readily in dogs after the administration of this drug. This led to a consideration experimentally of (1) the genesis and healing process of this type of ulcer, (2) the effect of a mechanical irritant and (3) the possibility of producing ulcer by the administration of cinchophen other than by the oral route.

REVIEW OF THE LITERATURE

Experimentally, the methods for the production of acute peptic ulcer have been many and relatively simple, while, on the other hand, the methods for the production of chronic peptic ulceration have been few and relatively difficult.

Churchill and Van Wagoner¹ (1931), in attempting to produce hepatic damage by the administration of cinchophen, noted from one to three gastric ulcers occurring in five of six dogs. The same authors² (1932) noted peptic ulcer in nineteen of twenty-four dogs which received cinchophen. The drug was mixed with the diet in amounts

*From the Division of Experimental Medicine, the Mayo Foundation.

1. Churchill, T. P., and Van Wagoner, F. H.: Cinchophen Poisoning. *Proc. Soc. Exper. Biol. & Med.* **28**:581-582 (March) 1931.

2. Van Wagoner, F. H., and Churchill, T. P.: Production of Gastric and Duodenal Ulcers in Experimental Cinchophen Poisoning of Dogs, *Arch. Path.* **14**:867-869 (Dec.) 1932.

varying from the dose for man to twenty-seven times that amount. The earliest ulcers developed in eight and ten days. In 90 per cent of the animals the ulcers were situated in the gastric pathway and were generally multiple. Ulcer of the first portion of the duodenum developed in four animals. The major symptoms noted were anorexia, occasional nausea and vomiting, tarry stools and loss of weight.

Churchill and Manshardt ³ (1933) injected cinchophen in cottonseed oil into the jejunum daily and noted gastric ulcer in three dogs. They concluded that the ulceration was not attributable to a direct, local, toxic action of the drug on the gastric mucosa.

Shoji ⁴ (1933), using sixty rabbits and fifty dogs, gave doses of cinchophen varying from 0.1 to 0.2 Gm. per kilogram of body weight enterally and parenterally for from one to seven hundred days. Catarrhal inflammation and erosion were noted in the rabbits' stomachs, and ulcers formed in the dogs' stomachs.

Barbour and Fisk ⁵ (1933), who studied hepatic damage in dogs after the repeated oral administration of cinchophen, noted gastric ulcer in some of their animals.

Hanke ⁶ (1934), seeking an explanation for the origin of the ulceration that follows the administration of cinchophen, gave a series of cats large subcutaneous doses of a cinchophen preparation. Grossly the stomachs showed linear defects throughout the mucosa, and in many instances acute erosions and ulcerations were present. There were microscopic changes in the cells throughout the stomachs, but the greatest destruction was in the peptic cells.

Schwartz and Simonds ⁷ (1935) gave cinchophen in oil orally to cats, rabbits and guinea-pigs. Superficial erosions and ulcerations were

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7. Schwartz, S. O., and Simonds, J. P.: Peptic Ulcers Produced by Feeding Cinchophen to Mammals Other than the Dog, *Proc. Soc. Exper. Biol. & Med.* **32**: 1133-1134 (April) 1935.

noted in the stomachs of the cats, but ulceration was not found in the stomachs of the rabbits or of the guinea-pigs.

Bollman and Mann⁸ (1935) fed 1 Gm. of cinchophen to normal dogs five days a week. They noted peptic ulcer as early as the first week and as late as the fourteenth month.

No cases have been reported in which undisputed peptic ulcer due to cinchophen affected man. Reah⁹ (1932) reported a case in which a patient died after therapy with cinchophen. Necropsy revealed a cirrhotic liver and a gastric ulcer. Bloch and Rosenberg¹⁰ (1934) suggested the possible etiologic relationship of the cinchophen. They¹¹ reported a similar case in which necropsy revealed hepatic damage, multiple gastric ulcers and chronic gastritis.

METHOD OF INVESTIGATION

Seventy-seven dogs with an average range of weight varying from 8 to 17 Kg. were used in these studies. Each dog was normal before the experiments were begun. All normal dogs can be considered not to have peptic ulcer, as statistics have shown that it is rarely if ever present. The animals were given the routine kennel care, and the majority were fed a diet composed of cracker crumbs, ground horse meat and evaporated skimmed milk. The diet consisted of a calculated weighed amount known to be sufficient to meet the caloric requirement of the dog and will henceforth be called the "regular diet." A few dogs were given the regular kennel diet for contrast. This is a coarser meal consisting of dog biscuits and a cooked mash.

All surgical procedures were performed with the dogs under surgical narcosis induced by ether, and careful aseptic technic was employed. All dogs that were killed were given a light ether anesthesia and were then bled from the femoral arteries. These and the dogs that died were examined thoroughly. The handling and fixation of the specimens were considered extremely important. The stomach was carefully opened along the greater curvature on the anterior wall. At no time was any portion that was to be sectioned washed or wiped. The entire organ was stretched out and pinned to a piece of stiff cardboard; it was then fixed in a diluted solution of formaldehyde U. S. P. (1:10) for forty-eight hours or more. Multiple sections of all the organs were also fixed in a similar solution. All ulcers and multiple blocks of tissue removed from scattered regions throughout the stomach and duodenum were embedded in paraffin. These were sectioned semiserially and stained with hematoxylin and eosin.

8. Bollman, J. L., and Mann, F. C.: Experimental Production of Gastric Ulcers, *Proc. Staff Meet., Mayo Clin.* **10**:580-582 (Sept. 11) 1935.

9. Reah, T. G.: Cinchophen Poisoning, *Lancet* **2**:504-509 (Sept. 3) 1932.

10. Bloch, Leon, and Rosenberg, D. H.: Gastric Ulcers Associated with Cinchophen Poisoning: Report of an Instance with Consideration of the Possible Etiologic Relationship, *Am. J. Digest. Dis. & Nutrition* **1**:29-31 (March) 1934.

11. Bloch, Leon, and Rosenberg, D. H.: Cinchophen Poisoning: Report of Seven Cases with Special Reference to Rare Instances Complicated by Multiple Gastric Ulcers, *Am. J. Digest. Dis. & Nutrition* **1**:433-437 (Sept.) 1934.

THE INCIDENCE OF PEPTIC ULCERS DUE TO CINCHOPHEN AND
THE EFFECT OF A MECHANICAL IRRITANT

Physical agents which traumatize the gastric mucosa have been thought to be an etiologic factor in peptic ulcer. Fauley and Ivy¹² (1930) found that coarse particles remain in the stomach longer than do fine particles. Obviously, the coarse particles produce prolonged motor activity of the stomach and an increase of trauma to an acute lesion of the mucosa. These investigators have produced chronic lesions from acute ulcers and have prolonged the healing time of acute lesions by feeding mechanical irritants.

Walker¹³ (1931) removed a portion of gastric mucosa from the stomach of several rabbits. A persistent mechanical irritant formed by a suture line directly beneath the lesion delayed the healing and increased the development of chronic ulceration.

Mann and others have demonstrated the presence of a mechanical factor in the production of peptic ulcer.

Our experiments on this phase of the subject follow:

Methods.—Fifty-one dogs were used in this study. These were divided into three groups. Group 1 consisted of twenty-eight dogs with an average weight of approximately 16 Kg. Twelve of them were fed the regular diet, and sixteen were fed this diet plus 100 Gm. of coarsely ground bone. The bone was given to determine the effect of mechanical irritation on the production and healing of the peptic ulcer. Regardless of the dog's size or weight, 2 Gm. of cinchophen well mixed with the diet was given daily to all animals. This is approximately three times the maximal daily dose for man and a fifth of the minimal lethal dose for dogs.

Clinically, the diagnosis of ulcer depended on the following symptoms: (1) vomiting of small amounts of gastric contents, (2) a tarry diarrhea of variable, but increasing severity, (3) anorexia, (4) anemia and (5) loss of weight and activity. If death did not occur at this stage from perforation of the ulcer, an exploratory operation was usually done and the presence of an ulcer confirmed.

Group 2 consisted of twenty dogs with an average weight of approximately 9 Kg. All were fed the kennel diet and were given 1 Gm. of cinchophen mixed with the meal daily five days a week. No drug was given the last two days of each week. It was intended in this way to determine the effect of the prolonged administration of a small dose of cinchophen. In every case the drug was given until the dog died or was killed.

Group 3 consisted of thirteen dogs. These were used as controls and did not receive any cinchophen. Three were fed the regular diet plus bone, and ten were fed the kennel diet. They were killed and examined after a longer period of observation than were any of the animals which received cinchophen.

12. Fauley, G. B., and Ivy, A. C.: Experimental Gastric Ulcer: The Effect of the Consistency of the Diet on Healing, *Arch. Int. Med.* **46**:524-532 (Sept.) 1930.

13. Walker, M. A.: Healing of Gastric Mucous Membrane in Rabbits After Its Surgical Removal, *Arch. Path.* **12**:85-89 (July) 1931.

Results.—GROUP 1.—Peptic ulcer developed in twenty-seven (96.4 per cent) of this group of twenty-eight animals. No animal was given cinchophen longer than sixty consecutive days. The one dog which did not have an ulcer did not reveal any noticeable effect of the drug.

Of the twenty-seven dogs which had an ulcer, nine (32.1 per cent) had multiple ulcers, and eighteen (64.3 per cent) had a single ulcer. All were gastric ulcers. Two (7.1 per cent) of the dogs had an associated duodenal ulcer. Twenty-five (89.3 per cent) had a pyloric ulcer situated from 2 to 3 cm. from the pyloric ring on the posterior wall and lesser curvature of the stomach (fig. 6). No ulcer was seen on the greater curvature. Frequently small contact ulcers were found about a large chronic ulcer. The multiple ulcerations were spread over the entire gastric mucosa but were most marked in the pyloric and fundic regions.

In the sixteen dogs that were fed bone, ulcer developed clinically in an average of seven days after the administration of 14 Gm. of cinchophen. Ulcer developed in eleven of the twelve dogs that were not fed bone in an average of eighteen days after the administration of 36 Gm. of cinchophen. The incidence of perforation was slightly higher, although not significantly so, among the animals which were fed bone. There were seven (43.7 per cent) perforations among the latter animals, as compared with four (33 per cent) among the animals that did not receive bone.

The condition of all animals at the time of necropsy was good; little alteration was observed in the nutritional state. In many instances the dog gained weight. Where there was a loss of weight, it was relatively insignificant, usually being from 0.5 to 1.2 Kg.

Roentgenographic studies were attempted for diagnostic purposes, but the difficulties encountered did not warrant the continuance of such studies. Roentgenoscopic examination of five dogs in this group revealed the presence of an ulcer in four of them. Exploratory operation revealed the presence of an ulcer in all of the five dogs.

GROUP 2.—Peptic ulcer developed in nineteen of the twenty dogs in this group (animals given 1 Gm. of cinchophen five days a week). The dog which did not have an ulcer received 281 Gm. of cinchophen in four hundred and eighteen days. This dog gained 5 Kg. and showed no noticeable effect of the drug. The animals in this group received an average total dose of 198 Gm. of cinchophen in two hundred and seventy days. The smallest dose was 22 Gm. in thirty days and the largest was 423 Gm. in six hundred and thirty days. Four of the dogs gained weight, but there was an average loss of 0.35 Kg.

Seven (35 per cent) of the nineteen dogs had multiple ulcers, and twelve animals (60 per cent) had a single ulcer. In every case there was a gastric lesion, although two dogs (10 per cent) had an associated duodenal ulcer. In seventeen instances (85 per cent) a chronic ulcer was situated in the pyloric region, on the posterior wall and the lesser curvature of the stomach. One animal (5 per cent) had an ulcer on the anterior wall of the stomach near the lesser curvature. No ulceration was observed on the greater curvature. Perforation occurred in two (10 per cent) of the dogs.

The time of development of the ulcers was variable. In two dogs exploration was done six months after administration was commenced, but no lesion was noted; six months later an ulcer was found in each animal. An ulcer was found in other animals on the twenty-second, sixty-first and one-hundredth day after administration of the drug, but one animal did not have symptoms until the six hundredth day.

GROUP 3.—The thirteen control dogs which did not receive the drug were normal in every respect. There was no macroscopic or microscopic lesion of the gastric mucosa of the three dogs which received bone in their diet.

Comment.—These studies demonstrate that the oral administration of cinchophen will produce peptic ulcer in nearly 100 per cent of all dogs. It seems logical that the presence of any mechanical irritant, such as bone, might cause microscopic damage to the mucosa, thus making it susceptible to early damage by cinchophen; or that the drug might cause the original injury and the trauma produced by the bone might aid in the development of the ulcer and production of early symptoms. The latter is more probable, because in no case were we able to demonstrate microscopic damage of the mucosa when cinchophen was not given.

No reason can be given for the failure of peptic ulcer to develop in two of the dogs.

That the general nutritional condition of the dogs was not responsible for the development of ulcer is significantly shown by the following findings: 1. Ulcer occurred in many dogs before any alteration in the nutritional state could be observed. 2. Many of the dogs gained weight; when there was a loss of weight, it was relatively insignificant.

It is interesting to note that perforated ulcer was less frequent in the animals which received doses of 1 Gm. of cinchophen than in animals which received larger amounts of the drug. This suggests that the smaller doses of the drug do not inhibit the healing processes as much as do the larger amounts.

A comparison of the situation of ulceration in man with that in animals is of interest. From 10 to 40 per cent of the peptic ulcers which affect man are multiple. From 70 to 95 per cent of the gastric ulcers which affect man are situated along the *Magenstrasse* in the pyloric region. These facts were found true of the ulcers which developed in the dogs. However, the number of gastric ulcers after the administration of cinchophen as compared to the number of duodenal ulcers is in exact reversal of the situation of peptic ulcer as seen in man. This is possibly attributable to the fact that the gastric mucosa of animals appears to be more affected by toxins than does the duodenal mucosa. The duodenal ulcers in the animals were in a situation comparable to that of the usual duodenal ulcer in man. Ulceration of the greater curvature is rarely seen in human beings, and it was not observed in the dogs.

THE EFFECT OF CINCHOPHEN WHEN ADMINISTERED OTHER WAYS THAN ORALLY

We have mentioned that peptic ulcer has been produced by the administration of cinchophen directly into the jejunum and parenterally. We administered cinchophen rectally, intravenously and subcutaneously

and by injection into an intestinal fistula to determine whether or not an ulcer would develop in the same manner as it did when the drug was given orally.

Injection into Intestinal Fistula.—Four dogs with an average weight of 15 Kg. and low jejunal or high ileal fistulas were used. Approximately 2 Gm. of cinchophen suspended in cottonseed oil was instilled daily through a catheter directly into the jejunum or ileum. Gastric ulcer, and in one instance, an associated duodenal ulcer, occurred in all four animals. The average time required for development of the ulcer was twelve days. There was no injury at the site of the injection of the drug.

Rectal Administration.—Two dogs weighing 19 Kg. were given a daily colonic irrigation; 4 Gm. of cinchophen in cottonseed oil then was instilled into the rectum. The animals showed symptoms referable to the action of the drug and were killed at the end of five days after the administration of the drug. Multiple acute gastric ulcers were found in both dogs. There was no injury to the rectum.

Parenteral Administration.—A neutral solution of the sodium salt of cinchophen was prepared for intravenous use. Each of two dogs, which weighed 18 Kg., was given an initial dose of 0.1 Gm. This was increased daily until a maximal dose of 2 Gm. had been reached. Definite symptoms were noted when a dose of 0.5 Gm. was given. These symptoms became progressively more severe as the dose of the drug was increased.

Immediately after the injection of 2 Gm. of the drug there were an increase in the nasal secretions, an increase in both the depth and the rate of respiration and an associated slowing of the beat of the heart. These symptoms were occasionally accompanied by involuntary micturition, forceful defecation and nausea and vomiting and rarely by a clonic twitching of the muscles. Fifteen minutes after the drug was given the symptoms disappeared, but the dogs remained stuporous for three hours. The most severe symptoms always occurred during the first hour. After the three hour period the animals appeared well and would eat as usual.

A more prolonged and a more gradual effect was desired; therefore, a daily subcutaneous injection of 2 Gm. of cinchophen suspended in cottonseed oil was substituted for intravenous administration. When the drug was thus administered, some symptoms were present by the end of the first hour. These reached their peak within three hours and gradually subsided during the next twelve hours.

Symptoms of ulcer developed in both dogs in one week. One dog was killed, and multiple acute gastric ulcers were present. The administration of cinchophen to the second dog was continued for an additional week. The dog was then killed. Two large subacute ulcers were found in the pyloric region on the lesser curvature and posterior wall of the stomach. There was an associated diffuse gastritis.

Two other dogs were given cinchophen intravenously for a period of less than one week. These were killed after one or two tarry stools had been passed. Microscopic lesions were found in the stomach of each dog.

THE DEVELOPMENT OF ULCER IN FUNDIC POUCHES

Method.—Fundic pouches were made in five dogs with an average weight of 11.5 Kg. This was done by cutting away a portion of the greater curvature of the stomach, forming it into a pouch and allowing it to drain through a de Pezzer catheter into a balloon which was carried at the side of the dog. These pouches were made primarily for a study of the gastric secretion, but in this paper mention will be made only of the results in regard to formation of ulcer.

Daily doses of cinchophen, which varied from 0.25 to 2 Gm., were mixed with the diet. The dogs were killed when they showed marked symptoms from administration of the drug or when the studies of the gastric secretion had been terminated.

Results.—Within four hours after 2 Gm. of cinchophen had been given orally, a small amount of macroscopic blood was present in the secretion in the pouch. The bleeding increased until the seventh hour. At this time the content of the pouch was cherry red. From the eighth to the twelfth hour after the oral administration of the drug, there was a rapid decrease in the amount of bleeding. Between the twelfth and the twenty-fourth hour, the secretion in the pouch was again clear. This same sequence occurred after each daily dose of cinchophen. The bleeding became progressively more severe, until at the time of definite formation of an ulcer there was some bleeding most of the time, but from the fourth to the twelfth hour after administration of the drug there was actually a hemorrhage. The amount of bleeding varied directly with the amount of drug given. The smallest dose of cinchophen that would produce an ulcer (0.5 Gm.) was the smallest dose that caused bleeding.

Ulceration developed in the pouches of all five dogs (fig. 1). Usually multiple, acute to subacute perforating lesions were found. In three animals the ulcer perforated the wall of the pouch. The other two had a microscopically perforating ulcer but were killed too early for gross perforation to occur. Ulcer formed in the pouch in from two to five days when the dose of cinchophen was 1 Gm. or more daily.

The stomachs in all five dogs were relatively free from injury, although superficial ulceration was noted at the lower end of the healed suture line (fig. 1) in four of the five dogs. There were also a few scattered linear erosions and mild gastritis. In no instance, however, was there a definite chronic ulcer in the stomach.

To determine whether or not cinchophen was being secreted into the isolated gastric pouches, several quarts of the secretion obtained from the pouches of dogs which were receiving cinchophen by mouth was concentrated by prolonged evaporation. This mixture was then subjected to a colorimetric test sensitive for cinchophen in amounts of from 0.01 to 0.1 Gm. A positive reaction was not obtained.

One quart of a mixture of the content of the pouch, which was not evaporated, was mixed with the diet of a dog which weighed 11 Kg. This was done daily for two weeks, and the stomach was then examined at necropsy. Ulceration was not found.

Comment.—These studies demonstrate that the administration of cinchophen by routes other than the mouth is equally effective in the production of peptic ulcer. They conclusively prove that the action of the drug is not local but occurs after absorption.

The rapidity with which symptoms appeared and then disappeared after the intravenous administration of the drug and the rapidity with which bleeding occurred in the fundic pouch and then as quickly subsided suggest that cinchophen is rapidly absorbed and rapidly excreted or destroyed. It is probable that the toxic effects and the excretion of the drug were nearly complete twelve hours after administration and were entirely complete after twenty-four hours.

The fact that acute ulcer occurred rapidly and was always of the perforating type in the fundic pouch lends support to the acid factor as

an important element in the production of the ulcer. The drainage of the pouch was never complete; no alkalinizing mechanism was present, and at most times there was some free acid in the contents. The stomach of each dog showed little injury. It seems likely that once the original mucosal destruction had occurred, the constant presence of the free acid in the pouch increased the rate of formation of ulcer.

The negative results obtained with the colorimetric test and the failure to produce ulcer by feeding the contents of the pouch to a dog suggest that cinchophen as such is not secreted by the gastric mucosa. It is possible that it may have been present in an amount too small to



Fig. 1.—Fundic pouch and stomach. Three acute ulcers and one subacute perforated (center) ulcer are seen in the pouch; in the stomach there is an erosion of the lower tip of the healed suture line.

detect with the method at hand or that it was present in a chemically changed form.

THE PATHOLOGIC STRUCTURE OF THE PEPTIC ULCER PRODUCED BY CINCHOPHEN

Van Wagoner and Churchill (1932) described the early ulcer due to cinchophen. They noted a destruction of the mucosa in the depth of a crypt. The mucosal cells were necrotic and covered with a layer of fibrin and polymorphic leukocytes. Radiating from the ulcer into the underlying tissue was an acute inflammatory reaction.

It is most frequently stated that peptic ulcer in man begins as a series of diffusely scattered acute ulcers. These tend to heal, and those in which the reparative process is less than the destructive process become chronic.

Mann¹⁴ (1925) observed the healing process in experimental peptic ulcers. He noted that there is first a clearing of the base of the ulcer and then the formation of a granulation tissue bud, which tends to fill the crater. At the same time there is a subsidence of the inflammatory reaction and a proliferation of the connective tissue. The mucosa then grows in from the edge and covers the granulation tissue as a single layer of epithelium. This layer rapidly becomes polypoid, and finally there is an atypical epithelium on a base of scar tissue.

Caylor¹⁵ (1926 and 1927) and Bliss¹⁶ (1932) reported a similar process in the healing of peptic ulcer in man.

Our experiments on this phase of the subject follow:

Methods.—Three dogs with an average weight of 17 Kg. were given 2 Gm. of cinchophen daily in a regular diet. Regardless of the presence or absence of symptoms, they were killed at intervals of five days. Multiple sections were taken from various regions of the stomach and duodenum. These were stained and studied microscopically for the presence of the early lesion.

In addition to these three dogs, all of the animals previously mentioned were used in this study. The diets and the doses of cinchophen which were administered have already been described. Each lesion was studied grossly and microscopically. To obtain the healing ulcer, exploratory laparotomy was performed; the presence of an ulcer was definitely confirmed, and its size and situation was determined. The administration of cinchophen was stopped on the day of the exploration. Postoperatively the dog was fed his previous diet without the drug. The animals were killed at definite periods, which varied from three days to twelve weeks after administration of the drug had been commenced. The specimens were treated and sectioned as described previously.

Results.—All of the specimens obtained from the animals used in this study were examined macroscopically and microscopically. These animals had received cinchophen in variable doses for variable periods of time. This afforded an opportunity for the study of the various stages in the development and the healing of ulcer. We have summarized these results and present them as a composite general picture.

The Early Lesion: Each dog that had had one or more tarry stools had a lesion of the gastric mucosa. A diffuse gastritis was usually present after the third or fourth dose of 2 Gm. of cinchophen (fig. 2). The entire stomach was

14. Mann, F. C.: Production and Healing of Peptic Ulcer, *Minnesota Med.* 8:638-640 (Oct.) 1925.

15. Caylor, H. D.: The Healing of Gastric Ulcer in Man, *Ann. Surg.* 83:350-356 (March) 1926; The Healing Process of Gastric Ulcer in Man, *ibid.* 86:905-917 (Dec.) 1927.

16. Bliss, T. L.: Healing of Chronic Duodenal Ulcers, *Am. J. Surg.* 15:93-98 (Jan.) 1932.

somewhat edematous and hemorrhagic in appearance. The mucosa was covered with an excess of mucus. Beneath this mucus and scattered over the entire mucosa, but chiefly throughout the fundic and pyloric regions, was an adherent layer of black altered blood. This appeared as a covering or as isolated pinpoint clots. Many of the clots were covered by folds of mucosa.

Multiple fine linear erosions were seen scattered between these blood clots. If a blood clot was removed, it was found that it filled one of these erosions. Occasionally there were superficial clean-appearing punched-out mucosal ulcerations. These usually were situated along the lesser curvature and varied from 1 mm. to 1 cm. in diameter.

Microscopically, sections through the area of gastritis demonstrated regions in which there were several necrotic mucosal cells sloughing into the lumen of the



Fig. 2.—A specimen showing diffuse gastritis. An edematous mucosa, with multiple adherent blood clots, a few linear erosions and small ulcerations are seen.

stomach (fig. 3). These were surrounded by a superficial inflammatory reaction, which consisted chiefly of polymorphonuclear leukocytes and involved only the mucosa. In many instances a bleeding mucosal blood vessel was noted. Throughout the stomach there were edema of the mucosa, a congestion of the mucosal blood vessels and an increase in the cellular elements, particularly of the round cells.

In the majority of instances the erosions rapidly developed into acute peptic ulcers. If a dog was killed during this acute ulcerative stage, from thirty to sixty acute gastric ulcers were found (fig. 4). These ulcers had a fresh and punched-out appearance. The edges were cleancut, smooth and not edematous. The floor of each ulcer was usually smooth, firm and clean but at times was covered by a thin layer of blood. No granulation or pus was seen on the surface of an ulcer. The size of the ulcers varied from 2 mm. to 1 cm. in diameter. The acute ulcers

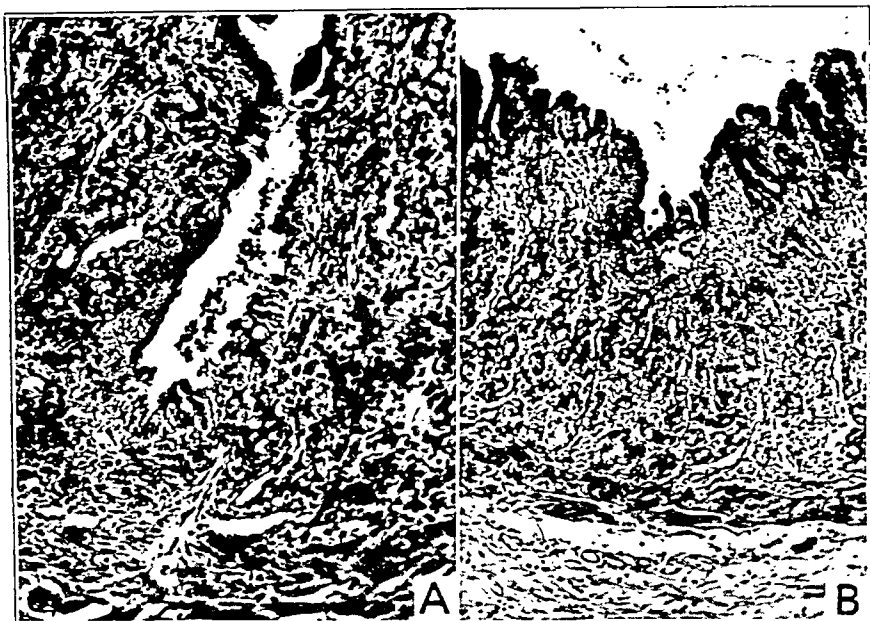


Fig. 3.—*A*, a photomicrograph of the earliest microscopic lesion, showing necrotic mucosal cells sloughing into the lumen of a crypt; $\times 120$. *B*, a photomicrograph of a slightly more advanced lesion than is shown in *A*, picturing destruction of the mucosal cells with a surrounding inflammatory reaction; $\times 85$.



Fig. 4.—A specimen showing multiple acute to subacute gastric ulcers.

usually involved only the mucosa and submucosa but at times involved all layers of the stomach and even perforated.

Microscopically, there was a sharply defined ulceration with a zone of neutrophilic infiltration in the floor of an ulcer (fig. 5). This frequently extended for a considerable distance below the necrotic layer, but for the most part the surrounding tissue had a healthy appearance. There was some edema, especially of the submucosa. The vessels were congested but showed no endothelial thickening. The muscle layer was frequently infiltrated with polymorphonuclear neutrophils.

The Late Ulcer: The multiple acute ulcers healed rapidly, and the diffuse gastritis disappeared. There persisted in the "ulcer-bearing" area a large chronic ulcer situated from 2 to 3 cm. from the pyloric ring on the lesser curvature and posterior wall of the stomach (fig. 6). Occasionally several acute to subacute

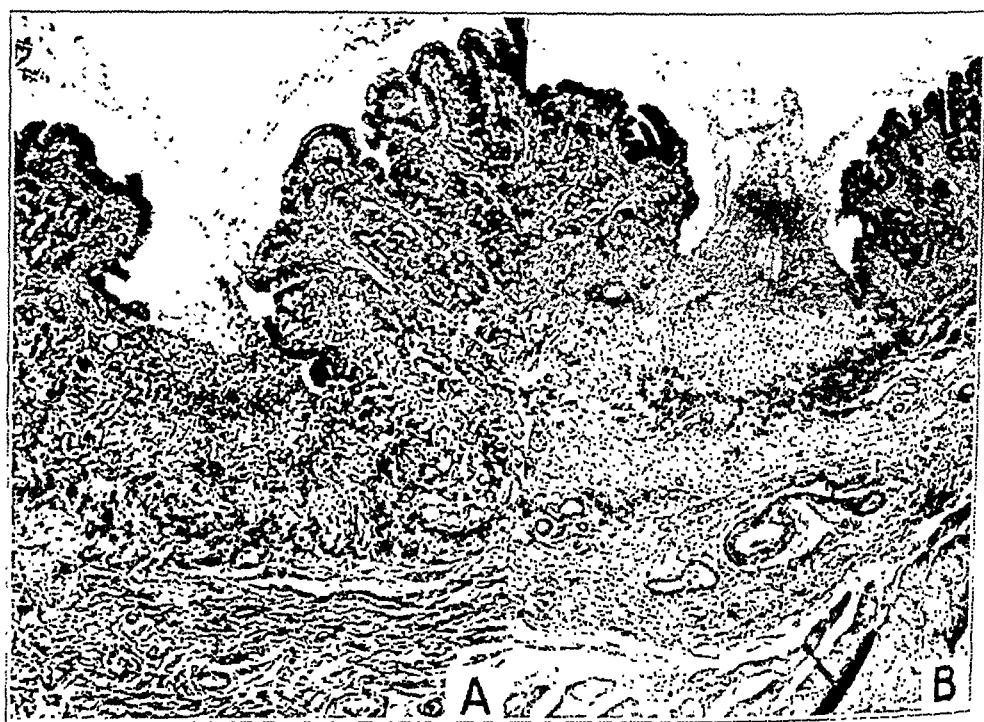


Fig. 5.—*A*, photomicrograph of an acute gastric ulcer with beginning involvement of the muscularis mucosa; $\times 60$; *B*, a photomicrograph of an acute gastric ulcer with involvement of the muscularis mucosa and beginning infiltration of the submucosa; $\times 30$.

ulcers were associated with this chronic ulcer, but there was never more than one chronic ulcer in a single specimen.

The chronic ulcer had an old appearance; it was thick, indurated and rounded and had overhanging edges. There was a dirty, necrotic or granulating floor. At times this floor was formed by the adjacent tissue, namely, the pancreas or liver. Occasionally there was a visible perforation through the base of the ulcer. This was associated with either a localized abscess or a general peritonitis.

Microscopically, there was a superficial zone of molecular necrosis (fig. 7) which rested on vascular granulation tissue. This granulation tissue was markedly infiltrated with fibrous connective tissue and lymphocytes. The muscle layer



Fig. 6.—A specimen showing a chronic perforated gastric ulcer on the lesser curvature of the stomach with multiple contact ulcers. Thirty-four grams of cinchophen was given in nineteen days.

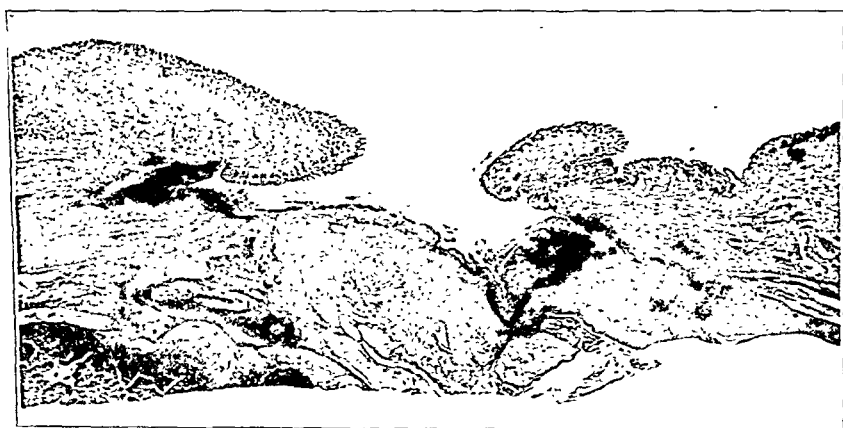


Fig. 7.—A photomicrograph of a chronic perforated ulcer of the lesser curvature of the stomach showing the undermined and rolled over edges, a superficial necrotic layer on a fibrous granulation tissue base and involvement of the omental fat and pancreas in the base; $\times 3\frac{3}{4}$.

was always penetrated and infiltrated with lymphocytes. In many cases the muscle had been replaced by the infiltrated pancreas or fibrous pads of gastrohepatic omentum.

The entire process extended for a short distance laterally. The blood vessels showed endarteritic and endophlebitic thickening with a large number of newly formed vessels. The general shape of the ulcer was variable but was usually funnel shaped or cone shaped.

At the margins of the ulcer there was evidence of proliferative activity on the part of the mucosal epithelium. The slough was lifted a bit or partially removed, and new mucosal cells were seen forming on a clean granulation tissue.

Healing Process: There was a constant attempt at healing in the peptic ulcer produced by cinchophen. When the administration of cinchophen was discontinued,

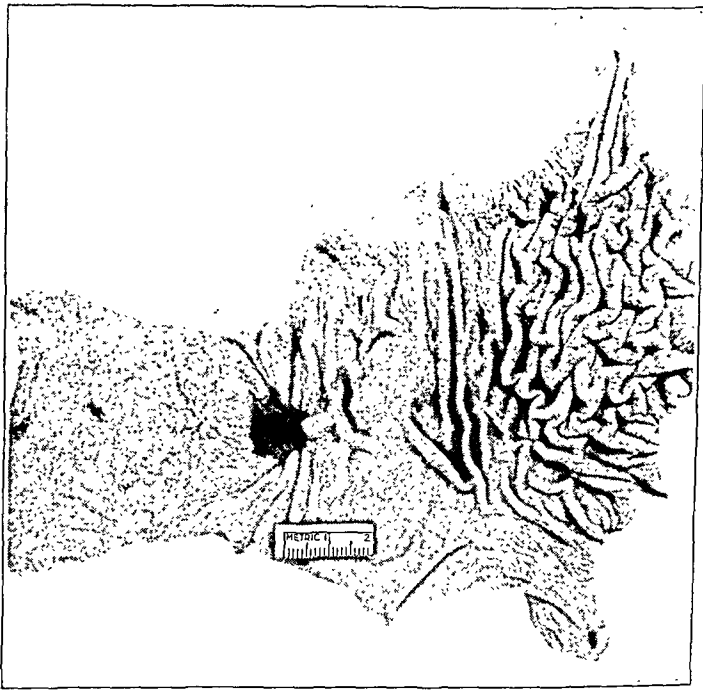


Fig. 8.—A specimen showing a chronic perforated ulcer of the lesser curvature of the stomach after two weeks' healing. The crater is nearly filled with clean granulation tissue; a fibrinous blood clot is seen in the center.

healing of the ulcer rapidly took place. This process was so rapid that no significant difference could be noted when the regular, the kennel or the bone diet was given. The time required for complete healing of the chronic ulcer was from three to five weeks. Complete healing was noted as early as two weeks, but some ulcers required more than seven weeks to heal. Occasionally the ulcer healed while the animal was receiving cinchophen. This was noted only in the dogs which received 1 Gm. of the drug five days a week. It was never noted in the dogs which received 2 Gm. of cinchophen daily.

Three days after the administration of cinchophen was discontinued the ulcer had a much cleaner appearance than before. The superficial necrotic layer had disappeared. The clean base was covered by a thin fibrinous blood clot. This clot disappeared at the end of one week after administration of the drug was

discontinued. The crater was being filled with vascular, friable, granulating tissue (fig. 8). By the tenth or twelfth day the granulation tissue had a polyp-like appearance and more than filled the crater. The mucosa could be seen growing over the granulation tissue from the edges of the ulcer.

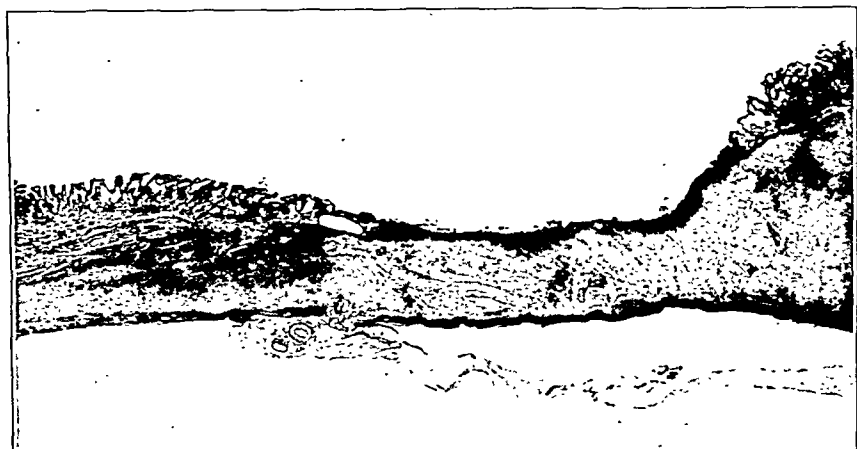


Fig. 9.—A photomicrograph of a chronic gastric ulcer after healing for one week; $\times 6$. One may note the clean granulation layer with the marginal epithelization.

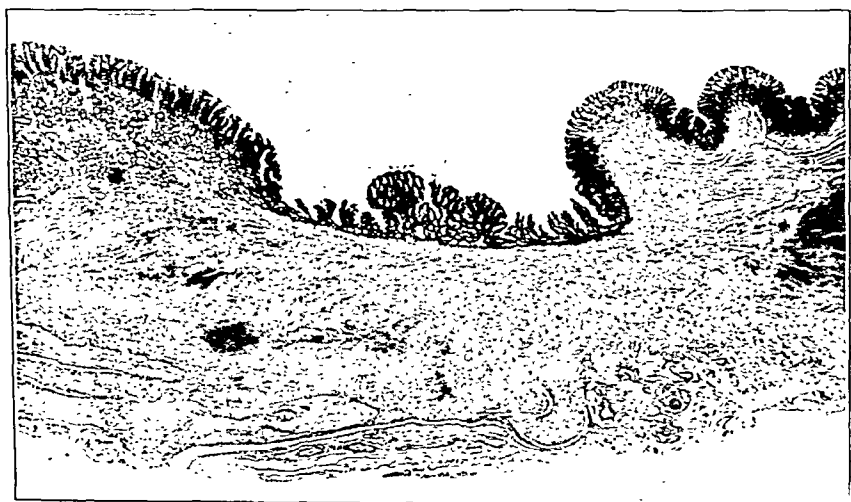


Fig. 10.—A photomicrograph of a chronic gastric ulcer during healing with newly formed mucosa becoming polypoid on a vascular scar tissue base; $\times 4\frac{1}{2}$.

Microscopic examination revealed the same changes as were seen grossly (fig. 9). In addition, a subsidence of the inflammatory reaction and marked proliferation of the fibrous tissue in the base of the ulcer were noted. The marginal

epithelium was seen growing as a single layer of flat or cuboidal cells over the granulating tissue. As this layer of cells progressed, the polyp-like projection of granulation tissue was pinched off. The new mucosal cells rapidly became columnar and were thrown into folds, which in turn formed villi (fig. 10). The mucosal glands then regenerated.

The damaged muscular layer was replaced by fibrosis. This fibrosis extended laterally beyond the defect and in some cases involved the serosa. Many of the blood vessels were obliterated, but many new ones were formed. The completely healed ulcer (fig. 11) was a scar-filled excavation covered by atypical epithelium.

Grossly, this completely healed ulcer (figs. 12 and 13) was recognized early by the raylike arrangement of the surrounding rugae. The regenerated epithelium had a whiter, more roughened and depressed surface than the surrounding mucosa.

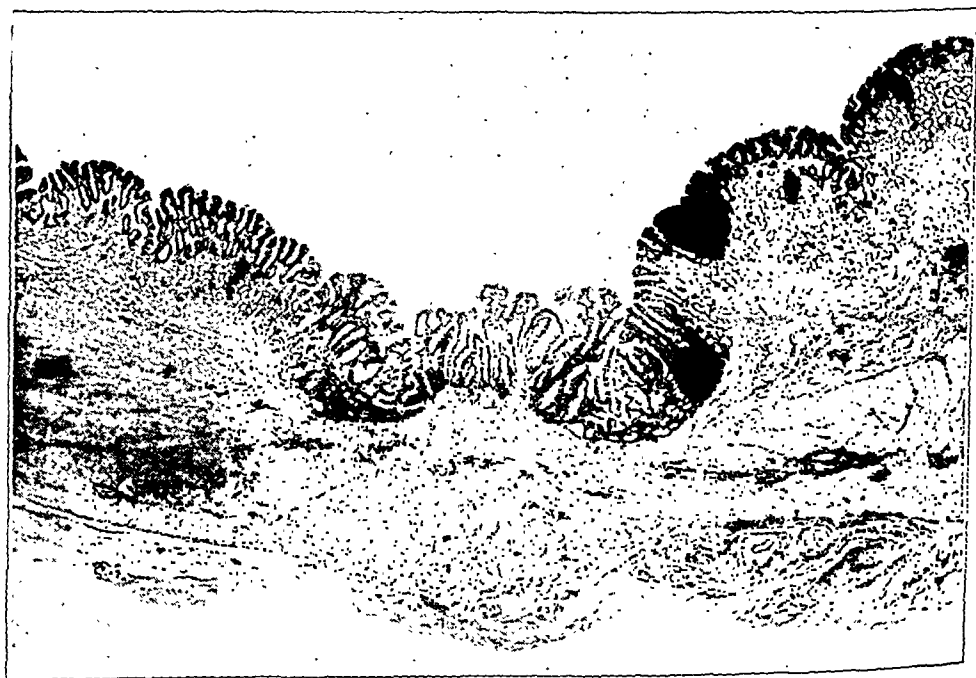


Fig. 11.—A photomicrograph of a completely healed chronic gastric ulcer, showing atypical mucosa on a scar tissue base; $\times 10$.

The healed ulcer was recognized with much greater difficulty at the end of twelve weeks. The mucosa appeared nearly normal, but there remained a persistence of the raylike rugae. Occasionally, the ulcer was recognized by the thickened white fibrous appearance of the serosal surface.

The majority of the dogs which were fed bone had particles of this bone embedded in the fibrotic layer of the healed ulcer. Several active ulcers contained hair, bone and other foreign bodies embedded in the base.

The gross and microscopic pictures of the duodenal ulcer are identical with those of the gastric ulcer.

Comment.—These studies demonstrate that the peptic ulcer produced by cinchophen begins with a destruction of mucosal cells. This occurs throughout the gastric mucosa and is associated with diffuse gastritis. There is hemorrhage from the mucosal blood vessels. The mucosal



Fig. 12.—A specimen with a chronic perforated ulcer on the posterior wall after six weeks' healing, showing the mucosa rolled from above over a small unhealed crater and spokelike contraction of the mucosal folds.

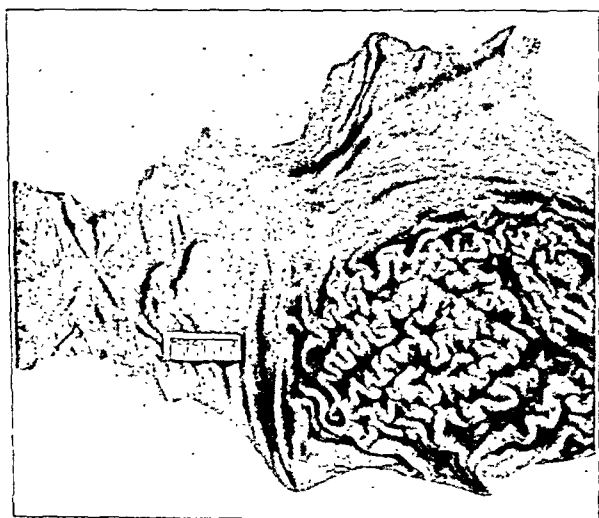


Fig. 13.—A specimen with a completely healed chronic perforated pyloric ulcer of the lesser curvature.

erosions progress as a result of digestion by the gastric contents and become multiple acute ulcerations. These acute ulcers heal, and the gastritis disappears. The acute ulcers in the gastric pathway, probably because of the trauma and increased digestion of tissue, progress and become chronic ulcers.

An ulcer heals rapidly when the administration of the cinchophen is stopped. The fact that the feeding of bone made no apparent difference in the rate of healing is interesting. It was shown that this traumatizing agent contacted the ulcer, because it was found embedded in the base of the ulcer. It cannot be definitely said that this irritant had no effect on the rate of healing, but there was none that could be accurately demonstrated. The etiologic factor was removed when the administration of the drug was stopped.

Pathologically, the peptic ulcer produced by cinchophen was identical in every respect with the peptic ulcer seen in man. The final true ulcer is a chronic lesion. This then gives us a method for consistently producing an experimental chronic peptic ulcer. This could be done consistently heretofore only by surgical means. This process presents itself as an invaluable one, because it opens up to a greater degree the possibility of experimental study of the chronic peptic ulcer.

SUMMARY

The administration of cinchophen is an effective method for the production of chronic peptic ulcer in dogs. Peptic ulcer developed in 95.8 per cent of the animals after the oral administration of cinchophen. A few duodenal ulcers occurred, but the majority of the ulcers were gastric. The use of bone as a mechanical irritant increased the rapidity of the formation of ulcer but did not demonstrably influence the rate of healing. Cinchophen administered by rectum, parenterally, through intestinal fistulas or orally to dogs which had fundic pouches produced peptic ulcer in all instances, which proved that ulcer occurred after absorption of the drug. The ulcer begins with an initial destruction of mucosal cells. The progression and healing are similar to those observed in other experimental peptic ulcer and in ulcer in man.

CEREBRIFORM NEVUS RESEMBLING CUTIS VERTICIS GYRATA

GEORGE HAMMOND, M.D.

AND

HENRY K. RANSOM, M.D.

ANN ARBOR, MICH.

The condition now known as cutis verticis gyrata was first described by Robert in 1848. The second example of this disease was recorded by Devergie (cited by Meirowsky) in his book "*Traité pratique des maladies de la peau*," which was published in 1854. In 1893 McDowell, an English neuropsychiatrist, described a similar case occurring in an epileptic microcephalic idiot. In the same year, Cowan reported 2 cases of the same nature, occurring in idiots. Jadassohn, at the Ninth Congress of the Dermatological Society in 1906, in Bern, presented a patient whose scalp in the occipital region was arranged in irregular folds, varying from 0.75 to 1.5 cm. in width. He later reported 2 additional cases. Unna in 1907 reported 3 cases of a similar nature. These cases were characterized by a gyrate appearance of the scalp over the vertex and the back of the head, resembling in appearance the furrows and convolutions of the cerebrum. He called the condition cutis verticis gyrata, and this name is the one most commonly employed today. Von Veress introduced the term "cutis verticis striata" to designate the 11 cases which were reported by him in 1908. In 1909 Audry introduced the name "pachydermie occipitale vorticellée" in describing his case. Stratton in 1933 found 158 cases reported by 87 different authors during a complete review of the literature on the subject.

GENERAL CHARACTERISTICS OF CUTIS VERTICIS GYRATA

Cutis verticis gyrata is a disease of the scalp characterized by the presence of a variable number of convolutions, or gyri, separated by furrows, or sulci. It is usually situated in the posterior parietal and occipital regions, although any portion of the scalp may be involved. The convolutions and furrows may be more or less parallel, running anteroposteriorly, from side to side or diagonally across. Less often they may be irregularly situated. The convolutions are permanent and ineffaceable, so that they can neither be made to disappear by traction on the skin nor be produced by pressure and counterpressure on the scalp. There are, in general, two main variables of this disease.

In the first type the gyri are less markedly elevated and merge imperceptibly into the adjacent normal scalp, a definite line of demarcation between the abnormal and the normal being absent. The maximum change is generally in the midline and extends symmetrically in all directions, becoming less and less marked as the periphery is approached.

The second type is characterized by a definite circumscribed tumor with raised abrupt borders. The convolutions in this type are more prominent and the furrows deeper, closely simulating the appearance of the cerebrum. The growth does not tend to be symmetrically situated. Another distinguishing feature is that it occurs more frequently in females and is usually present from birth. This type is caused by a nevus, usually of the pigmented variety. Slow growth is the rule, although periods of more rapid growth are not uncommon. Whereas the first type is usually inconspicuous and discovered accidentally, the second type forms a prominent tumor mass which is obvious to the patient for a long time.

ETIOLOGY AND CLASSIFICATION OF CUTIS VERTICIS GYRATA

For many years considerable confusion and disagreement existed in the minds of various authors concerning the exact etiology of cutis verticis gyrata. This was largely due to the fact that it was not generally recognized that this disease may be related to several different etiologic factors.

In 1893 McDowell suggested that the cutaneous folds were due to hypertrophic muscles of the scalp, similar to the folds noticed when a dog "pricked his ears." It seems reasonable to assume that in some cases cutis verticis gyrata represents a reversion to a period when the muscles of the scalp could move the scalp at will. Fischer (1922) expressed the belief that the anomaly in certain cases is developmental and is comparable to the conditions present in the scalps of many mammals, such as lions, tigers and bulldogs. The occurrence of cutis verticis gyrata in idiots tends to support these views.

Jadassohn in 1906 and Unna in 1907 regarded the condition as the result of an anomaly of development and classified their cases as belonging to the larger general group of nevi. This view was supported by Silvestri (1909) and Rouvière (1911). Malartic and Opin (1914) and Lenormant (1920) definitely established the nevic nature in their cases by histopathologic examination. Various inflammatory diseases of the scalp were considered as the etiologic agents by von Veress in 1908 and by Audry in 1909. In 1911 Sabat reported a case associated with acromegaly, and Adrian (1916) and Grönberg (1927) suggested a causal relationship between the two diseases. Galant (1918) and Stühmer (1922) expressed the belief that the condition in their cases had developed on a traumatic basis.

Von Veress (1908), Pospšelloff (1909) and Wise and Levin (1918) found cutis verticis gyrata associated with syphilis. It was not demonstrated by any of these observers that an actual syphilitic infiltration of the scalp was responsible for the abnormality, although a generalized syphilitic infection was present at the time the patients were first examined. Fischer in 1922 advanced the theory that in some cases the condition could be explained on the basis of an anomalous and apparently congenital hypertrophy of the connective tissue of the scalp. Oliver in 1922 offered the explanation that in time a chronic inflammatory process in the scalp produces fibrous tissue, which by contracting gives rise to furrowing of the scalp. Pelagatti (1924) described a case in which the anomaly was due to a leukemic infiltration of the scalp. Truffi (1930) reported a case in which pemphigus seemed the causative factor.

In 1933 Stratton argued that the anatomic construction of the scalp might explain the condition, since so many unassociated causes apparently resulted in the same deformity. He stated that in the scalp strong fibrous bands run diagonally and perpendicularly through the fat, firmly connecting the galea aponeurotica and the skin. It was conjectured that the fat was replaced by the infiltrating cells but that the fibrous bands were not. This resulted in gyri and sulci, or the formation of cutis verticis gyrata. He thought that the size of the gyri depended directly on the intensity of the infiltration.

Fischer (1922) greatly simplified the entire subject of cutis verticis gyrata by offering an etiologic classification which served to correlate the many conflicting views regarding etiology. His classification is as follows:

A. True cutis verticis gyrata—a developmental anomaly representing a reversion to a lower form of life when the muscles of the scalp could move it at will.

B. Diseases of the scalp "in the form of" cutis verticis gyrata.

1. Inflammatory changes, acute and chronic, e. g., eczema, psoriasis, folliculitis and impetigo.
2. Anomalous and apparently congenital hypertrophies of the connective tissue.
3. Tumors, such as nevi and neurofibromas.
4. Changes in the scalp occasioned by diseases that lead to proliferation of the tissues, such as acromegaly, myxedema, leukemia and cretinism.

To this classification might be added:

5. Changes in the scalp resulting from trauma.

In the present study, reports of 117 cases of cutis verticis gyrata were found in the literature. We have attempted to group these cases according to Fischer's classification. There were 9 cases of true cutis verticis gyrata, forming 8 per cent of the total. Eighty-five cases of diseases of the scalp "in the form of" cutis verticis gyrata were found, aggregating 72 per cent of the entire number. In 22 cases, or 19 per cent, the data given were insufficient to permit an accurate classification.

Of the 85 cases which fell into the second group, 26 (22 per cent) were caused by inflammatory changes; 4 (3 per cent) resulted from anomalous and apparently congenital hypertrophy of the connective tissue; 24 (21 per cent) were due to neoplasms, all of which were nevi; 26 (22 per cent) were occasioned by diseases that lead to proliferation of the tissues, and 6 (5 per cent) were consequent on trauma.

The 26 cases occasioned by diseases that lead to proliferation of the tissues have been further subdivided into 19 cases associated with acromegaly, 1 case caused by a leukemic infiltration of the scalp, 4 cases apparently due to syphilis and 2 cases in cretins.

HISTOLOGIC PICTURE OF CUTIS VERTICIS GYRATA

Naturally, the histopathologic picture of the disease will vary according to the etiologic agent.

We have found no observations on the histopathologic picture in cases of true cutis verticis gyrata or in cases of changes in the scalp in the form of cutis verticis gyrata resulting from trauma. Neither have we noted any observations concerning the histopathologic picture in cutis verticis gyrata occasioned by diseases that lead to proliferation of the tissues.

Von Veress (1908), Vignolo-Lutati (1910) and Hannay (1923) have reported their microscopic observations in cases of cutis verticis gyrata following inflammatory diseases of the scalp and, in general, their descriptions are in agreement. According to them, the epidermis exhibited no change. In the deeper parts, infiltrations of plasma, lymph and mononuclear cells could be seen, often localized about the deeper follicles. Von Veress reported a complete disappearance of elastic fibers. Atrophy of the sebaceous and sweat glands occurred in some cases, while von Veress found a disappearance of the sebaceous glands in his cases. No excessive pigment formation was seen.

The histopathologic picture in the group of cases caused by an anomalous and apparently congenital hypertrophy of the connective tissue is self-explanatory. Ota (1931) found hyperplasia of the sebaceous glands with a thickening of the connective tissue of the cutis.

Tumors in the form of cutis verticis gyrata have been described by various authors. Malartic and Opin (1914) and Lenormant (1920) saw large numbers of nevus cells beneath the epidermis as the characteristic feature in their cases. Alderson (1927) found dense collections of pigment in the upper layer of the corium and large whorls or cords of connective tissue in the lower layer. No nervous tissue was seen. Grieve and Biddle (1931) noted pigmented nevoid cells just beneath the epidermis. In their cases the connective tissue was very cellular and vascular and was arranged in concentric bundles or whorls, especially well marked in the deeper layers of the corium. Madden (1935) reported an unusual case of cutis verticis gyrata due to a melanoma which had undergone malignant degeneration.

ORIGIN AND NATURE OF THE NEVUS

For many years there has been a divergence of opinion as to the origin of the nevus. There are, in the main, two schools of thought on the subject. One considers the nevus to be of mesodermal origin, and the other, of ectodermal origin. Each theory has been strongly supported by recognized investigators.

It is of interest to review a more recent conception of the origin of the nevus because this view seems entirely plausible and is being more and more widely accepted today.

Soldan in 1899 observed the association of nevus cells with sensory nerve elements and advanced the opinion that the nevus, like a neurofibroma, was formed by proliferation of the connective tissue of the sensory nerves of the skin. The pigmentation was considered to be a consequence of this fibromatosis.

Recently, by special staining methods, Masson (1926, 1931, 1932 and 1933) presented convincing evidence to show that the nevus and the melanoma are formed not by an abnormal proliferation of the connective tissue of the nerve sheaths but by a proliferation of the ends of the cutaneous sensory nerves. He expressed the belief that in the dermis the nevus cells arise from the cells of Meissner's corpuscles; that in the epidermis they come from the specialized tactile corpuscles of Merkel-Ranvier, and that they originate from the special pigment cells known as chromatophores in both situations. He has observed many features of nevus formation in the pigmented spots in the skin in Recklinghausen's disease and has found miniature neurofibromas in connection with nevi. He, therefore, accepts the relation of the nevus to neurofibromatosis. It is Masson's opinion that all nevi are neuronevi and that all are neuromatous terminations of tactile nerves. This theory serves to harmonize the ectodermal and mesodermal theories of origin and is supported by Ewing (1928), Stout (1932), Foot (1932), Weller (1936) and many others.

TREATMENT OF CUTIS VERTICIS GYRATA

The treatment of this disease has depended greatly on the etiology and nature of the abnormality. No treatment has been advocated for those cases not caused by a nevus, except for the treatment of the underlying disorders such as inflammatory diseases, myxedema, acromegaly, etc. The literature contains no report of a cure of cutis verticis gyrata of this type after improvement or cure of the causative factor. As a rule, surgical treatment is not indicated, because, first, there is little demarcation between the normal and the abnormal scalp, so gradually does the one blend into the other; and, secondly, the patient does not desire radical treatment for a lesion causing so little inconvenience and deformity.

However, in those cases in which the condition is caused by a nevus, one is dealing with a circumscribed, deforming tumor which has malignant potentialities. As for a nevus elsewhere, the treatment is surgical. There are two types of procedure: (1) complete excision with subsequent skin grafting, if a primary closure cannot be effected, or (2) gradual partial excision with closure. The latter method was advocated by Davis in 1934 in the operative treatment of hemangioma.

Davis stated that this method is of value when the growth cannot be entirely removed at one operation with immediate primary closure, either because the defect is too large or because it is in a situation where there is insufficient lax tissue to allow an immediate closure. We have found it a worth-while method in treating a large nevus of the scalp. In this procedure an elliptic incision is made in the tumor, and as much of the growth as possible is removed, but not enough to interfere with immediate closure of the wound. According to Davis, after healing is complete, in order to allow stretching of the surrounding tissues, at least two months should elapse before the second operation. This is carried out in exactly the same manner, and the procedure is continued with similar intervals until the growth is completely eradicated. During the intervals massage is helpful in stretching the skin. The objection may be raised that the trauma caused by partial excision might possibly result in malignant degeneration. It is an alternative method that may be used in certain cases in which the condition does not lend itself to complete excision with subsequent primary closure or skin grafting.

In this discussion it is of interest to note the differences of opinion among different writers as to the most satisfactory form of treatment of a nevus. These methods of therapy range from the application of the electric needle, solid carbon dioxide, cautery, caustics, radium and liquid air to electrolysis, roentgen irradiation, endothermy, electrodesiccation and electrocauterization. We believe that the best form of treatment is complete surgical excision.

REPORT OF CASES

Two cases of cerebriform nevus of the scalp resembling cutis verticis gyrata have recently been observed at the University Hospital.

CASE 1.—H. K., a 9 year old white American school girl, was admitted to the clinic on July 25, 1933, complaining of a growth on the side of the head. This lesion had been present since birth and had been increasing in size recently. It caused her no discomfort, but the parents desired its removal for cosmetic reasons.

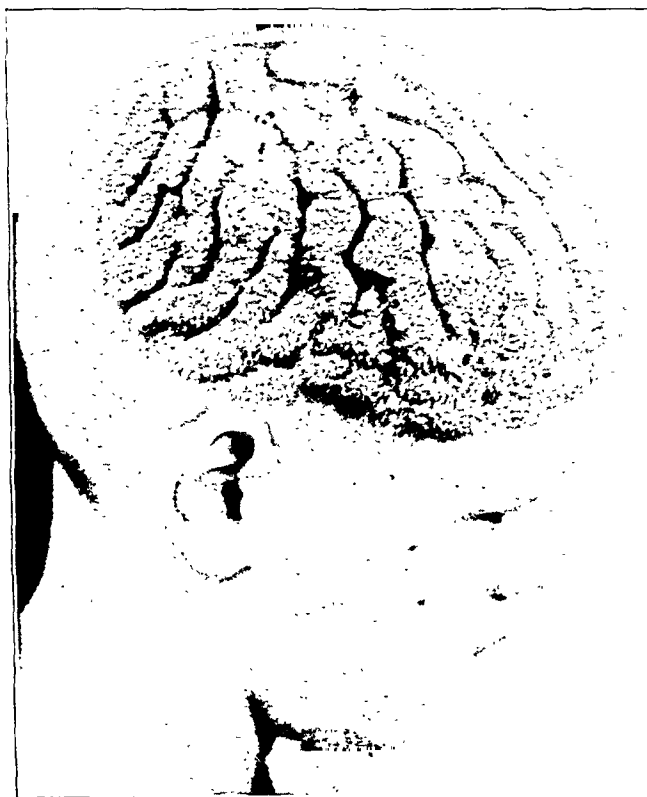


Fig. 1 (case 1).—Cerebriform nevus of the scalp resembling cutis verticis gyrata.

There was no history of any other disease of the scalp or of injury to the scalp. The patient had no other complaints.

Her past history was essentially irrelevant. There was no history of a similar deformity in either parent and no history of syphilis.

Physical examination revealed a healthy, well developed, well nourished girl of normal mentality. A circumscribed tumescence covered with hair presented itself on the right parietofrontal region of the scalp. It was approximately 15 cm. long and 12 cm. wide and extended from the vertex to within 1 inch (2.5 cm.) of the right ear and from the occipital region posteriorly to the hair line of the forehead

anteriorly. This tumor was composed of multiple gyri separated by rather deep furrows and was distinctly demarcated from the surrounding scalp by its raised abrupt edges. The gyri were rather soft and closely resembled cerebral convolutions. One portion of the growth exhibited a violaceous color. The tumor was not attached to the underlying bone. There was no evidence of inflammatory disease of the scalp. Whitish particles the size of a pinhead were attached firmly to the hair (figs. 1 and 2).

The remainder of the physical examination revealed nothing significant.

The results of the laboratory examinations were negative. The hemoglobin content was estimated to be 80 per cent (Sahli); the leukocytes numbered 6,400 per cubic millimeter. The urine was normal, and the Kahn reaction of the blood was negative. Roentgen examination of the skull revealed no bony abnormality.



Fig. 2 (case 1).—The nevus as seen from the front.

Diagnoses of pigmented nevus of the scalp and pediculosis capitis were made, and surgical excision was advised.

Accordingly, on August 10, with the patient under anesthesia with tribromethanol in amylene hydrate and nitrous oxide curved vertical incisions were made through the central portions so as to excise an ellipse of the tumor. The tumor tissue showed no unusual vascularity. The edges of the tumor were then mobilized and sutured together with black silk, obliterating the operative defect. The tumor tissue removed measured 15 by 6.5 cm. Convalescence was uneventful. The wound healed by primary intention, and the patient was discharged on September 2.

She was readmitted to the hospital on November 11. The history for the interval between discharge and admission was unimportant. Examination revealed no change in the character of the tumor except for the diminution in size, resulting from the first partial excision. On November 11, with the patient anesthetized

with tribromethanol in amylene hydrate and nitrous oxide, an elliptic sagittal incision was made through the temporal part of the mass, extending down to the pericranium. The ellipse of tumor was then removed. The edges of the skin were approximated without undue tension and sutured with interrupted black silk. This portion of the tumor measured 15 by 3 cm. The postoperative course was without event, and the patient was discharged on December 1.

She returned on June 12, 1934, giving an unimportant history for the interval between discharge and admission. Examination gave negative results, except for the presence of the remaining portion of the tumor. On June 16, the same type of anesthesia being used as before, a narrow elliptic incision was made in the sagittal direction of the scalp, and the remaining portion of the tumor was excised. The edges of the skin were mobilized and closed without undue tension with black



Fig. 3 (case 1).—The operative scar and areas of hyperpigmentation in the surrounding skin. These cannot be seen when the hair is dressed naturally.

silk. This portion of the tumor measured 15 by 3 cm. The convalescence was entirely satisfactory, and the patient left the hospital on June 27.

A check-up examination on August 22 revealed an excellent result.

The patient was last seen on March 20, 1935 (fig. 3). There was no indication of recurrence, and the result was satisfactory. The scalp in the region of the operative scar revealed areas of hyperpigmentation, which disappeared at the hair line and were not visible when the hair was normally dressed.

The histopathologic description of the excised tissue was as follows (Dr. C. V. Weller): "The highly convoluted scalp is covered by an atrophic squamous epithelium beneath which there are many nests of typical nevus cells, producing large amounts of melanin. In the deeper portions, the proliferation assumes a pronounced fibroblastic character with a whorling architecture, so that, in many fields,

the appearances are those of a typical neurofibroma with all the intervening nevoid gradations being demonstrable. In the neurofibromatous portion, no melanin production occurs. This is a pigmented nevus, showing very beautifully the combination of neurofibromatous areas and medullary nests of nevus cells" (fig. 4).

CASE 2.—M. L., a 22 year old white American woman, was admitted to the University Hospital on May 29, 1934, complaining of a tumor on the back of her head and swollen glands in the neck. The growth had been present since infancy and had slowly increased in size. Two months before entrance to the hospital the growth had become painful, and she had noted chills and fever. She thought that one portion of the tumor had become infected and had "drained" for a short time.



Fig. 4 (case 1).—Superficial medullary nests of nevus cells producing melanin and more deeply situated neurofibromatous areas ($\times 24$).

At that time the glands of the right side of the neck had become tender and swollen and had remained in that condition. Her history was otherwise noncontributory. There was no history of syphilis, inflammatory disease of the scalp or trauma to the scalp. The patient had been overweight for many years.

Physical examination revealed a very obese white woman, appearing the stated age of 22 and having a normal mentality. There was an unusual tumor situated in the posterior portion of the scalp. It was an elevated, circumscribed growth, roughly circular in outline, extending from the vertex to the lower occipital region, posteriorly and to within 1 inch of either ear laterally. It was orange-red and measured 25 cm. in its greatest vertical diameter and 20 cm. in its greatest horizontal diameter. The surface was elevated 2 cm. above the surrounding scalp.

It presented many rubbery, firm nontender nodules and convolutions separated by furrows which, in part, greatly resembled convolutions of the cerebrum. The hair was rather thick in the sulci and sparse over the surface of the convolutions. The tumor was movable over the underlying skull. No inflammation was present. The cervical lymph nodes in the right anterior and posterior triangles were slightly enlarged and tender (fig. 5). The remainder of the physical examination revealed nothing significant. The examinations of the blood and urine gave essentially negative results. The Kahn test of the blood was negative.

Diagnoses of nevus of the scalp and obesity were made.

Due to the depth and firmness of the convolutions in various parts of the tumor, complete excision with subsequent skin grafting seemed to be the procedure of

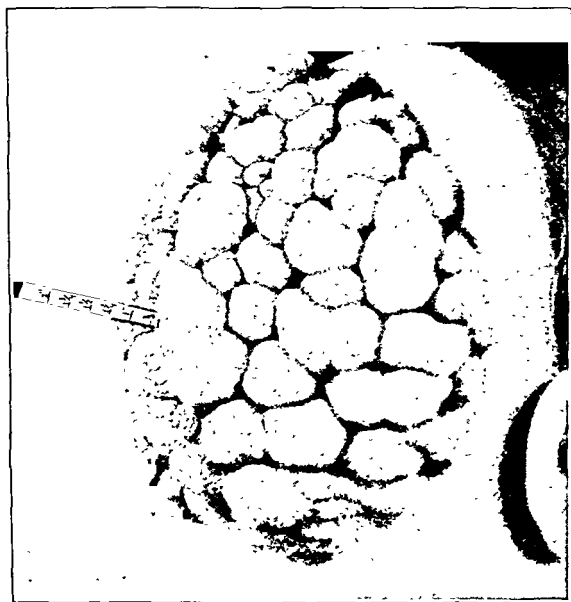


Fig. 5 (case 2).—Cerebriform nevus of the scalp resembling cutis verticis gyrata.

choice. Therefore, on June 4, the patient being anesthetized with tribromethanol in amylene hydrate and nitrous oxide, a circular incision was made about the periphery of the tumor, which was then elevated. A definite line of cleavage was found in the subaponeurotic space, and the tumor was thus easily removed. The edges of the skin were sutured to the pericranium to prevent retraction. Bismuth tribromphenate was used in dressing the wound (fig. 6). The convalescence was uneventful. On June 23, with the patient under nitrous oxide anesthesia, split thickness skin grafts were taken from the posterior aspect of the right thigh and applied to the denuded area on the posterior aspect of the scalp by suturing them to each other and to the surrounding skin. A sea-sponge pressure dressing was applied. The grafts were successful (fig. 7). The donor areas on the thigh were epithelialized completely in about twelve days. The patient was discharged from the hospital on July 28.

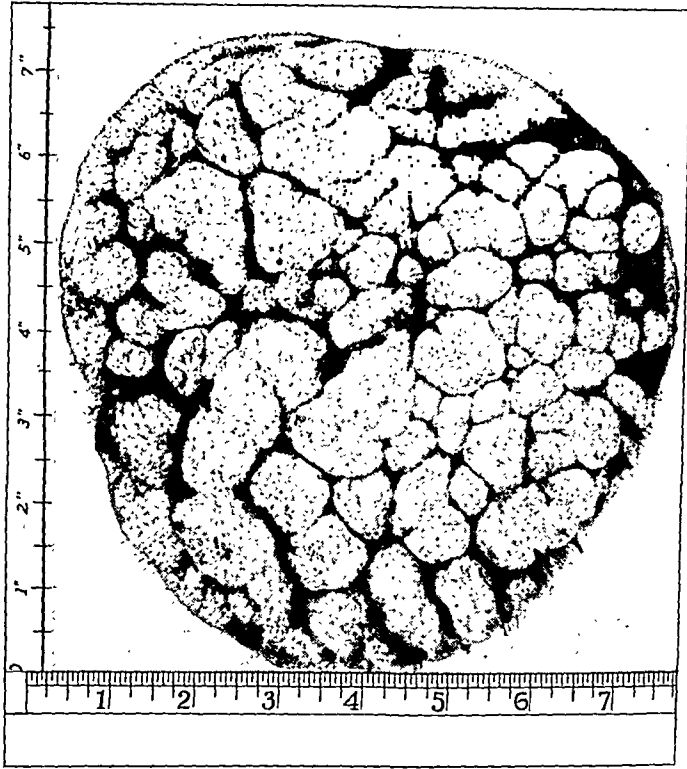


Fig. 6 (case 2).—Appearance of the nevus after its removal.

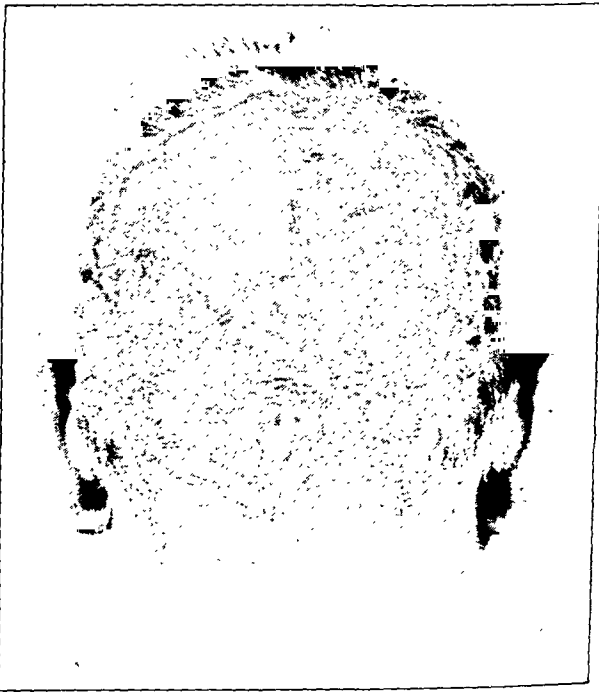


Fig. 7 (case 2).—The operative defect covered by skin grafts.



Fig. 8 (case 2).—Photomicrograph of the nevus ($\times 24$).

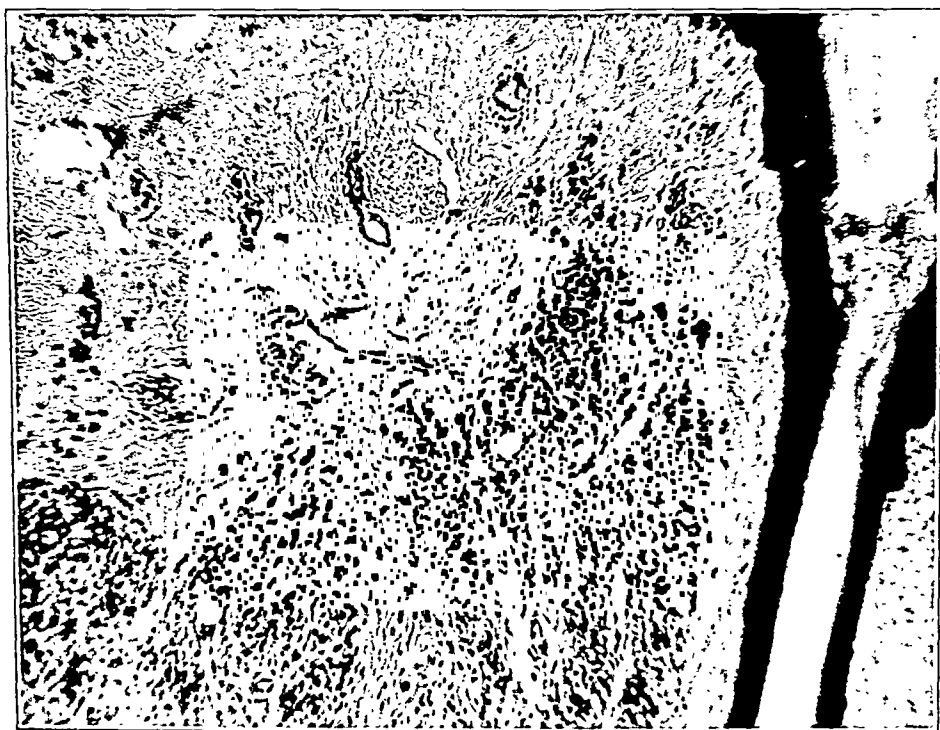


Fig. 9 (case 2).—Photomicrograph showing the nevus cells close beneath the epithelium ($\times 110$).

On March 15, 1935, she reported by letter that she was well and that there had been no sign of recurrence.

The histopathologic description of the neoplastic tissue was as follows (Dr. C. V. Weller): "The scalp is thrown into convolutions by a marked thickening of the corium. There is a widespread proliferation of nevus cells, many of which grow in small nests and cords close beneath the papillomatous squamous epithelium. In the deeper portions, the proliferation assumes a markedly fibroblastic character, whorls of stroma containing elongated cells with spindle-shaped and ovoid nuclei being prominent. In these regions, the appearances suggest those of a neurofibroma" (figs. 8, 9 and 10).



Fig. 10 (case 2).—Photomicrograph of a deeper portion showing the neurofibromatous areas ($\times 110$).

COMMENT

As already indicated, the particular nevus of the scalp reported here constitutes a condition distinctly different, both clinically and pathologically, from all the other types of cutis verticis gyrata. Since this condition presents so few features in common with cutis verticis gyrata, we suggest that it be removed from this classification and designated as cerebriform nevi of the scalp. An interesting commentary in this connection is the fact that in the literature and textbooks this convoluted nevus is referred to as cutis verticis gyrata when it occurs on the scalp.

but as nevus cerebriformis or cerebelliformis when it occurs elsewhere on the surface of the body.

As suggested by Madden (1935), cutis verticis gyrata should be considered a descriptive term only, and it should be generally understood that several different pathologic processes in the scalp may result in the formation of convolutions and furrows. In any patient exhibiting cutis verticis gyrata, a careful differential diagnosis should be made to determine the underlying cause so that appropriate treatment can be recommended.

We believe that Masson has shown rather conclusively that a nevus represents a proliferation of the chromatophores, tactile corpuscles and nerve cells, forming the end-apparatus of the sensory nerve filaments of the skin. There seems to be little doubt of the relationship of the nevus to the neurofibroma. The results of the histopathologic study in the 2 cases herein reported support Masson's concept of the neurogenic nature of the nevus.

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FRACTURES OF THE ANKLE

GEORGE APFELBACH, M.D.

Attending Surgeon, Cook County Hospital

AND

LEON BOIM, M.D.

CHICAGO

During the period from 1932 to 1934 there were admitted to the fracture service for females at the Cook County Hospital patients with 3,294 fractures. The fractures, dislocations and tears in the ligaments of the ankle numbered 352, or 10.84 per cent of all fractures. These were reduced and treated subsequently in the follow-up clinic. Our data are based on the records of the hospital and the follow-up clinic and on our study of 300 of the hospital's roentgenograms.

We are adding to these data the results of a study of 78 fractures of the ankle encountered in private practice, with a review of the roentgenograms. Our work, therefore, is based on a study of 430 fractures of the ankle and a review of the roentgenograms of 378.

The clinical study of these fractures has been augmented by a detailed description of the practical anatomy and physiology of the ankle joint by one of us (L. B.).

Even after employing the accepted methods of treatment of Pott's fracture and other injuries to the ankle, the results, such as faulty weight bearing, pes planus, limitation of motion, widening of the mortise and arthritic and circulatory changes, have motivated the study.

We propose to clarify confusion in the classification, anatomy and mechanism and to advocate an additional manipulation in the reduction of fractures with dislocation.

ANALYSIS OF DATA

The incidence of fractures of the ankle at the Cook County Hospital for the three year period was as follows:

	Total Fractures	Fractures of the Ankle	Percentage
1932	1,024	95	9.5
1933	1,070	99	9.2
1934	1,155	158	14.0
	<hr/> 3,249	<hr/> 352	<hr/> 10.84

On the basis of the type of fractures we classified the 300 fractures studied roentgenographically as follows:

	No.	Percentage
Pott's fracture (figs. 8, 9, 12, 13, 14, 15, 16, 17 and 22)	225	75.0
Supination fracture (fig. 19)	15	5.0
Bimalleolar fracture (fig. 10)	28	8.5
Solitary marginal fracture	3	1.0
Compression fracture (fig. 11)	5	1.6
Simple fracture (fig. 20)	21	7.3
Epiphysial separation (fig. 18)	3	1.0

We further subdivided the fractures of the ankle as follows:

A. Pott's fracture	225
Uncomplicated (figs. 8, 9, 15, 16, 17 and 22)	157
With a Tillaux fragment (small marginal fracture)	27
Anterior (fig. 14)	1
Posterior (fig. 15)	24
Anterior and posterior	2
Anterior marginal	6
Posterior marginal (fig. 12)	30
Anterior and posterior marginal (fig. 23)	5
B. Supination fracture	15
Uncomplicated (fig. 19)	9
With a Tillaux fragment (posterior)	1
Anterior marginal	2
Posterior marginal	0
Anterior and posterior marginal	1
With fracture heads of the fibula	1
With epiphysial separation	1
C. Bimalleolar fracture (fig. 10)	28
Uncomplicated	20
With a Tillaux fragment	0
Anterior marginal	1
Posterior marginal	6
With epiphysial separation	1
D. Solitary marginal fracture	3
Anterior	0
Posterior (2 without dislocation)	3
E. Compression fracture (fig. 11)	5
F. Simple fracture one or both maleoli (without any dislocation)	21
External malleolus (fig. 20)	17
Internal malleolus	3
External malleolus and anterior marginal	1
G. Epiphysial separation (fig. 18)	3

In the roentgenograms of 300 fractures of the ankle we noted the following involvement of the bones:

External malleolus	150
Internal malleolus	109
Both malleoli	57
Fibula, above the joint	183
Oblique fracture of the fibula	153
Posterior marginal fragment	39
Anterior marginal fragment	9
Both Tillaux and marginal fragments	63
Tillaux fragment (posterior)	27
Both anterior and posterior marginal fragments	3

It is interesting to note the following facts:

1. Pott's fracture occurred in 75 per cent of our series but was complicated by some form of marginal fragment in 30 per cent. We consider this complication higher in females than in males, probably because the former wear high heels.

2. Solitary marginal fracture is uncommon, occurring only 3 times in 300 roentgenograms and from our records of 352 cases. This is less than 1 per cent of fractures of the ankle. In only 1 of these was there a posterior dislocation, so that 2 of these might have been classified as simple fractures.

3. The most common fracture was Pott's fracture, in which there is an oblique and sometimes a spiral fracture of the fibula running downward and forward. This constituted 50 per cent of all our fractures. It is the most common fracture of the ankle. In about 10 per cent of these there was also involvement of the external malleolus.

4. In supination or fractures with medial dislocation, we noted in addition to fracture in the fibula or external malleolus a longitudinal fracture of the tibia or a spiral fracture in the shaft of the tibia.

The incidence of dislocations was as follows:

Lateral dislocation	157
Posterior dislocation	45
With lateral and posterior dislocation	36
Upward dislocation (compression)	5
No dislocation	21
Reduction of fracture before taking roentgenogram (mostly Pott's fracture)	36
Diastasis noted roentgenographically	117

The clinical facts in this series of fractures are summarized briefly:

The time of fixation for uncomplicated Pott's fracture averaged five and one-half weeks; for lateral and posterior displacement, seven weeks; for all types, six weeks.

Two or more reductions were required in 30 cases.

There were 6 compound fractures. In 2 of these cases extension on a Braun or Böhler splint was used.

Extension with a Kirschner wire or a Steinmann pin was used 6 times.

The length of time before weight bearing was allowed averaged in all cases about ten weeks; for uncomplicated Pott's fracture, eight weeks; for Pott's fracture or bimalleolar fracture with posterior dislocation, eleven weeks; for posterior marginal fractures, eleven and one-half weeks.

Results were markedly good in 168 fractures, fair in 33, poor in 15 and undetermined in 84. These data depend entirely on the examiner's opinion. Measurements made by one of us on 50 fractures of the ankle showed an increase in the circumference of the ankle at the malleoli in 47. Note that in 300 roentgenograms diastasis was found in only 117, or 40 per cent, whereas widening of the mortise was observed in 94 per cent as a clinical end-result. In many of these there was pes planus, and in many others the roentgenograms showed fairly good position.

In reviewing the films and records of 78 cases encountered in private practice, we note the following distribution of fractures:

	No.	Percentage
Pott's fracture	38	49.0
Supination	2	2.5
Bimalleolar fracture	6	7.0
Solitary marginal fracture	2	2.5
Compression fracture	1	1.3
Simple fracture	29	37.0
Epiphysial separation	0	0.0

In this series, as compared with those at the Cook County Hospital, there were more uncomplicated Pott's fractures and more simple fractures. In the 2 posterior marginal fractures there were no posterior dislocations.

In looking over the films we found a single instance of injury to the ankle, clinically accompanied by swelling and pain but no fracture. There were, however, considerable diastasis and widening in the mortise. We found no cases of dislocation without fracture. Diastasis probably occurs in many cases of sprain and is a cause of later disability.

There were 21 multiple fractures in our series.

ANATOMY AND PHYSIOLOGY OF THE ANKLE JOINT

Only such anatomic points will be presented as bear on our views of the mechanism of fractures of the ankle.

Inferior Tibiofibular Syndesmosis.—The distal extremities of the tibia and fibula articulate by surfaces which are for the most part rough

and bound together by ligament, but at the distal part, for a distance of about $\frac{1}{4}$ inch (0.6 cm.), they are separated by a cleft, continuous with the cavity of the ankle joint, which is lined by synovial membrane and commonly contains a synovial fold.

The ligaments of this articulation are: 1. The anterior lateral malleolar (anterior inferior tibiofibular) ligament (fig. 1). This ligament extends obliquely downward and outward, is about $\frac{3}{4}$ inch (1.9 cm.) wide and is attached to the external and anterior angle of the lower extremity of the tibia; it is attached to the fibula along the

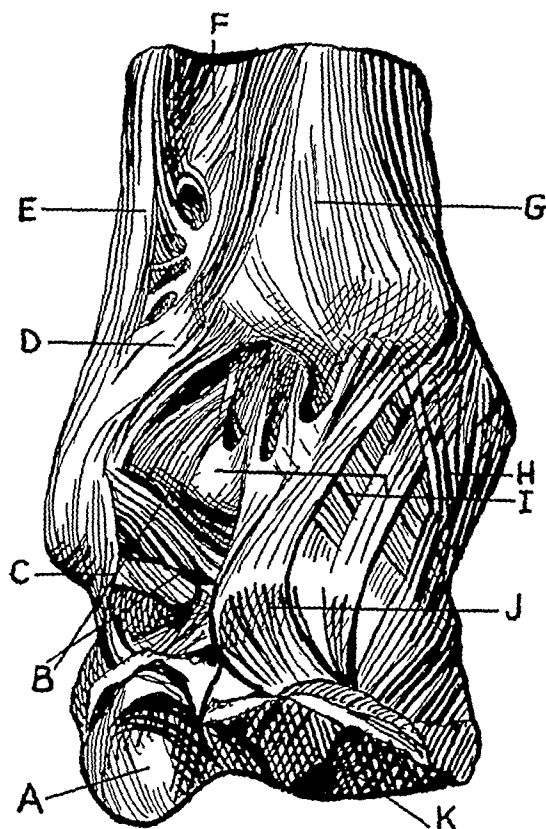


Fig. 1.—Anterior view of the ankle joint (modified after Bourguery: *Traité complete de l'anatomie de l'homme comprenant de la médecine opératoire*, Paris C.-A. Delaunay, 1832-1854). *A* indicates the calcaneum; *B*, two bands of the anterior talofibular ligament; *C*, the exterior lateral ligament; *D*, the anterior inferior tibiofibular ligament; *E*, the fibula; *F*, the interosseous ligament; *G*, the tibia; *H*, the internal lateral ligament; *I*, the anterior ligament of the ankle joint; *J*, a prominence formed by the astragalus, and *K*, the scaphoid.

lower $\frac{1}{2}$ inch (1.3 cm.) of the ridge in front of the superficial triangular surface of the bone; to the anterior surface of the malleolus, nearly down to the anterior portion of the external lateral ligament of the ankle, and to a part of the anterior ligament of the ankle. The fibers of the ligament increase in length from above downward.

2. The posterior lateral malleolar ligament (fig. 2). This ligament extends from the external angle of the posterior surface of the lower end of the tibia, downward and outward to the fibula, along the lowest $\frac{1}{2}$ inch (1.3 cm.) of the ridge separating the posterior from the external surface and to the upper half of the posterior border of the external malleolus.

3. The transverse ligament (fig. 2). The posterior lip of the tibial plafond projects so low as to have been called by Destot the posterior malleolus. The transverse tibiofibular ligament, located beneath

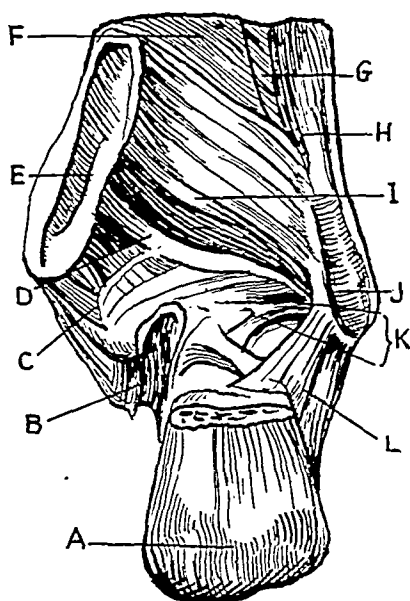


Fig. 2.—Posterior view of the ankle joint (modified by Bourger). *A* indicates a posterior tubercle of the os calcis; *B*, a groove on the astragalus for the flexor hallucis longus tendon; *C*, the internal lateral ligament; *D*, the transverse ligament; *E*, a groove for the flexor digitorum longus and the tibialis posterior tendons; *F*, the tibia; *G*, the inferior interosseous ligament; *H*, the fibula; *I*, the posterior inferior tibiofibular ligament; *J*, a groove for the peroneus tendons; *K*, the posterior fasciculi of the external lateral ligament, and *L*, the middle fasciculus of the external lateral ligament.

the posterior inferior tibiofibular ligament, extends from the posterior lip of the tibia to the posterior and inner angle of the base of the external malleolus. Another way of describing this ligament is that the distal part of the posterior inferior tibiofibular ligament forms a strong band, which takes a transverse course and is firmly attached to both the tibia and the fibula. It constitutes a part of the tibiofibular

socket for the talus at the ankle joint and is sometimes called "the distal ligament of the lateral malleolus."

4. The inferior interosseous ligament (figs. 1 and 2). This ligament consists of a dense mass of short fibers, passing transversely between the opposed lower ends of the tibia and the fibula, except for $\frac{3}{8}$ inch (0.9 cm.) at the extremity of these surfaces, where there is a synovial cavity. The ligament extends from the anterior to the posterior inferior tibiofibular ligaments. In front it reaches upward for $1\frac{1}{2}$ inches (3.8 cm.), but behind, only about half that height.

The synovial cavity of this articulation communicates with that of the ankle joint. It is semilunar, with its convexity upward, where it is limited by the lower end of the inferior interosseous ligament.

*The Ankle Joint Proper.*¹—This is a hinge joint, and the distal extremities of the tibia and the fibula are united so as to form a three-sided socket, which receives and embraces the talus. The socket is completed opposite the interval between the tibia and the fibula by the lower part of the anterior lateral malleolar ligament (mentioned previously) in front and by the transverse ligament behind. It is broader in front than behind, and its posterior margin is placed on a lower level than the anterior margin. An irregular archway is thus formed by the two bones of the leg, under which is received the astragalus, the outer buttress, which is the longer, being formed by the fibula, while the inner buttress and the span of the arch are formed by the tibia.

Ligaments of the Ankle Joint.—A capsular ligament invests the joint; it is thin in front and behind but is supported on each side by strong collateral ligaments. This capsular ligament, being attached in places beyond the astragalus, assists in forming the capsules of some of the tarsal joints. There are four named ligaments: the anterior, posterior, internal and external lateral.

The anterior and the posterior ligaments need no description.

The internal lateral ligament² (fig. 3), erroneously named the deltoid ligament, is a quadrilateral mass of vertical, coarsely fasciculated fibers, descending from the tibia to be attached posteriorly to the astragalus and anteriorly to the sustentaculum tali. The anterior part of this ligament is strengthened by fascia (partly derived from the internal annular, or laciniated, ligament), which fashions it into a deltoid structure. After reaching the sustentaculum tali, the true ligamentous fibers interlace with the upward and forward passing fibers of the supero-internal calcaneonavicular ligament.

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The external lateral ligament (fig. 4) consists of three parts. (a) The anterior portion is connected with the anterior border of the external malleolus just below the point of attachment of the anterior ligament of the ankle. Below it is fixed to the astragalus in front of the facet for the fibula. (b) The middle fasciculus is attached to a portion which passes as a groove round the inferior border of the external malleolus, slightly in front (but not to the tip), and passes downward to a tubercle on the outer surface of the os calcis. (c) The posterior fasciculus, probably the strongest of all, is attached at one end to the border of the external malleolus, which separates the peroneal groove

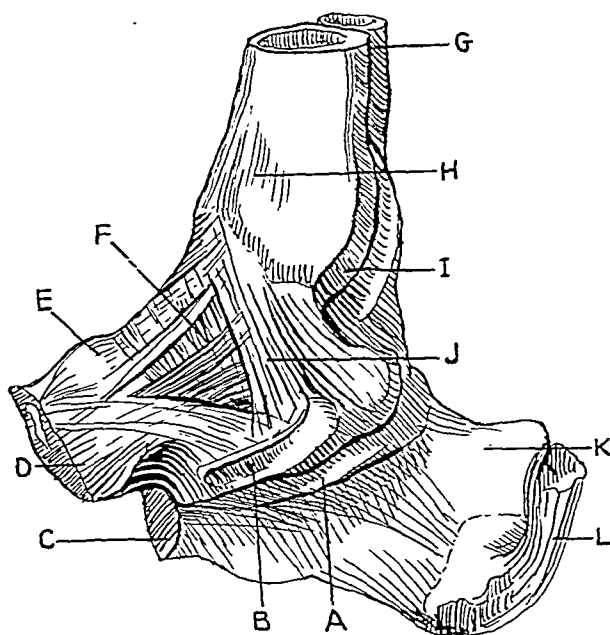


Fig. 3.—Medial aspect of the ankle joint (modified after Bourguery). *A* indicates the groove for the flexor digitorum longus and the flexor hallucis longus tendons; *B*, the groove for the tibialis posterior tendon; *C*, the calcaneus; *D*, the scaphoid; *E*, the astragalus; *F*, parts of the internal lateral and anterior ligaments of the ankle joint; *G*, the fibula; *H*, the tibia; *I*, the groove on the tibia for the flexor digitorum longus; *J*, the interior lateral ligament; *K*, the calcaneum, and *L*, the tendo Achilles.

from the fossa on the inner surface, and slightly to the lower part of the fossa itself, and at the other end to the rough outer surface of the astragalus below and to the articular facet for the fibula behind and also to the posterior external tubercle of the astragalus. This groove and depression for the posterior fasciculus constrict and weaken the bone. In accidents, because of the enormous strength of this pos-

terior fasciculus, holding the astragalus almost indissolubly attached to the external malleolus, either the fibula gives way, which is usual, or the posterior tubercle of the astragalus is detached. This lateral tubercle of the posterior process of the astragalus, or os trigonum, is present as a distinct bone or additional ossifying center in 7 or 8 per cent of cases. It is located from 5 to 7 mm. posterior to the median tubercle and is the portion of the astragalus which casts the farthest posterior shadow in lateral roentgenograms of the foot.

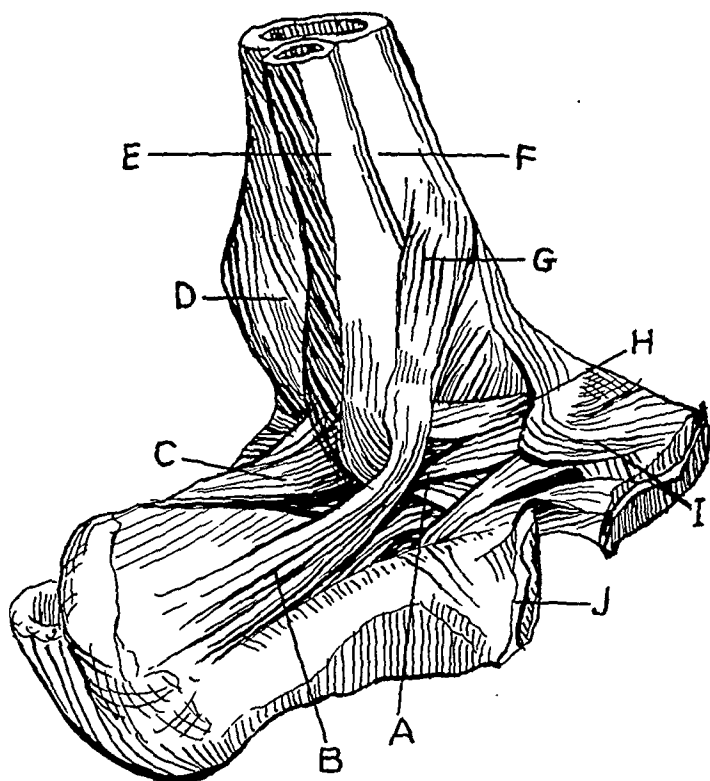


Fig. 4.—Lateral view of the ankle joint (modified after Bourguery). *A* indicates two bands of the anterior talofibular ligament; *B*, the middle fasciculus of the external lateral ligament; *C*, the posterior band of the external lateral ligament; *D*, the tibia plus part of the posterior inferior tibiofibular ligament; *E*, the fibula; *F*, the tibia; *G*, the anterior inferior tibiofibular ligament; *H*, the anterior band of the exterior lateral ligament; *I*, the scaphoid, and *J*, the calcaneum.

The synovial membrane of the ankle joint is extensive. It lines all the ligaments and sends upward a short cul-de-sac for the inferior tibiofibular joint. On the anterior and posterior surfaces it extends beyond the limits of the articular facets. The epiphysial line of the tibia is $\frac{1}{2}$ inch (1.3 cm.) above the level of the ankle joint in front and about $\frac{5}{8}$ inch (1.5 cm.) above posteriorly, so that the synovial membrane does not reach this line on either aspect. The epiphysial line of the fibula is from $\frac{3}{4}$ to $\frac{7}{8}$ inch (1.9 to 2.1 cm.) above the tip of

the external malleolus and is almost 1 cm. below that of the tibia, lying in a direct horizontal line with the opposed articular surfaces of the tibia and the astragalus. This epiphysis, then, lies almost exactly on a level with the plane of the ankle joint. The synovial membrane overlaps the diaphysis of the fibula for about 0.5 cm.

Bony Configuration.—(a) Lower End of the Fibula: The external malleolus supports the ankle joint on the outer side, projecting down and more posterior than the internal malleolus. The result of this is that the foot may receive, in the best possible way, shocks transmitted to it from above.

(b) Shaft of the Tibia: This part of the bone is twisted; when the tibia is placed on its posterior surface it rests on the posterior edges of both its condyles but on the posterior and lateral edges only of its lower articular end, the inner malleolus being turned away from the supporting surface. This twist in the tibia gives an outward slant to the foot from the heel, causing the great toe to incline away from that of the opposite side when the heels are placed in contact. A line drawn from the point of the heel through the middle or longest toe coincides with the plane in which the foot moves in flexion and extension on the leg. The direction of this movement, therefore, is oblique with regard to that of the knee joint and to that of the plane in which the leg bones descend from the knee. The movement of the ankle joint takes place in a perpendicular plane on an axis, which passes from left to right through the lower part of the astragalus and which is the center of a circle of which the upper articular surface of the astragalus forms a segment.

(c) Astragalus: The whole of the upper, outer and inner surfaces and the greater part of the posterior surface of this bone assist in forming the ankle joint, either by smooth cartilaginous facets for articulating with the bones of the leg or by rough surfaces for the attachment of the ligaments. Of the three facets, we shall consider the superior only for our present purpose. This occupies the posterior two thirds of the upper surface of the bone; it is arched considerably, being decidedly narrower behind than in front and longer on the inner than on the outer side; the outer border is higher and more prominent, especially in front, so that there is a slight inward obliquity given to this upward looking facet.

From this description the fact can be appreciated that in extreme extension, or plantar flexion, there is a twisting of the toes inward and that is partly due to: (1) the greater posterior length of the inner border of the superior articular surface of the astragalus; (2) the lesser proportionate height posteriorly of the outer border of that

surface, the hindmost part of which is in plantar flexion brought into the tibiofibular arch, and (3) also partly the lateral movement in the calcaneo-astragaloid joints.

The movements of the foot on the leg are varied and difficult to analyze, because they pass easily into one another; because, as Humphry³ stated, two or more are generally combined, and because they are divided between three distinct joints. These are (1) the joint between the tibia, fibula and astragalus; (2) the joint between the astragalus and the os calcis, a double joint having two separate synovial cavities, and (3) the joint between the first and the second row of tarsal bones—between the astragalus and the os calcis behind and the scaphoid and the cuboid bone in front—which is also a double joint.

Flexion and extension at the ankle joint take place around a transverse line drawn through the body of the astragalus. The movements are not in a direct anteroposterior plane but along a plane inclined outward and drawn through the foot from the middle of the astragalus to the opposed surfaces of the bases of the second and third metatarsal bones. This oblique plane corresponds to the outward inclination of the toes, to the slight twisting of the shaft of the tibia and to the posterior position of the external malleolus. For the sake of brevity we may say that the axis of movement of the ankle joint passes approximately through the end of the fibular malleolus. Thus the middle fasciculus of the external lateral ligament can be more or less tense throughout the range of movement, but the anterior and posterior fasciculi, being attached to the fibula away from the axis, are of more value in limiting movement and become tense in plantar flexion and dorsiflexion, respectively.

There is a slight lateral movement of the foot in ordinary plantar flexion, owing partly to the fact that the internal malleolus is shorter than the external and partly to the narrower end of the astragalus being in that position brought into the widest part of the intermalleolar notch.

Muscles Acting on the Ankle (Directly or Indirectly).—It is well known that no single muscle can produce simple flexion or extension of the foot without producing abduction or adduction at the same time.

1. The gastrocnemius and the soleus (spoken of together as the triceps surae) are the extensor-adductor muscles. They act by stretching the back part of the foot and the outer half of the forepart of the foot; they act in the plane of movement of the ankle by means of the tendo Achillis, which plane may, for simplicity, be said to be passing through the os calcis, the middle of the ankle joint and the space between the two inner metatarsal bones.

3. Humphry, G. M.: *A Treatise on the Human Skeleton (Including the Joints)*, Cambridge, Macmillan & Co., 1858.

2. The peroneus longus is the extensor-abductor muscle; the action of this muscle, combined with that of the triceps surae, causes direct extension of the foot at the ankle.

3. The tibialis anticus is the flexor-adductor muscle.

4. The extensor digitorum longus is the flexor-abductor muscle; the action of this muscle, combined with that of the tibialis anticus, causes direct flexion of the foot.

5. The tibialis posticus is a pure adductor muscle.

6. The peroneus brevis is a pure abductor muscle.

However, as pointed out by Cyriax (1917). Haines (1935) and others, some muscles have full action and others short action; the latter are those in which the length of the fibers is so short that they do not remain taut throughout the full range of movement permitted by their attachments; these include the biceps femoris, semimembranosus, rectus femoris, gastrocnemius, plantaris and soleus muscles. For example, when the ankle is in full plantar flexion and the knee is also flexed, the lower part of the leg not touching the ground, the tendo Achillis is slack to palpation. The only active muscles appear to be the tibialis posticus and peroneus muscles.

NOMENCLATURE OF THE MOVEMENTS OF THE ANKLE AND FOOT

There is a good deal of diversity of opinion concerning the nomenclature of the movements of the ankle and foot. We fully concur with the contention of Professor Thane,⁴ who claimed that although the foot in the position of rest is more or less at right angles with, and projects both in front of and behind, the bones of the leg, the two projections are not of equal value. The axis of the limb is continued in the anterior projection, and the projection of the heel is a secondary prominence, which does not occur in the primitive form. The angle between the leg and the forepart of the foot is, therefore, the angle to be considered. A diminution of this angle is flexion, and an increase of this angle is extension, in accordance with what would universally be understood by "straightening the foot upon the leg." The terms flexion and extension are physiologic terms, and it is desirable that they should be used only in a physiologic sense. The direction at which the bending at a given joint takes place is determined by the functional requirements of the part. In the upper limb all the joints are bent in the same direction, in accordance with the use of the limb as a grasping organ. In the lower limb the large joints are bent in

4. Thane, G. D., in discussion on Humphrey, G. M.: *J. Anat. & Physiol.* 28: xv-xvi, 1893-1894.

opposite directions alternately, that arrangement being the most convenient for the shortening of a column of support. We therefore conclude with most authorities that plantar flexion is extension of the foot and dorsiflexion, flexion of the foot.

Other movements are described in connection with the ankle and foot; these, however, belong not to the ankle but to the subastragaloid joints.

The movements of pronation of the foot consist of the horizontal rotation of the astragalus with the sinking of its head, the rotation in valgus of the os calcis beneath it and the rotation in valgus and abduction of the front part of the foot as a whole, occurring between the astragalus and the scaphoid and between the os calcis and the cuboid bone. The head of the astragalus moves in a ball and socket joint formed by the sustentaculum tali, the calcaneoscaphoid ligament and the scaphoid. It moves inward and backward toward the sole, and this is accompanied by the very oblique change in position of the malleoli, which, of course, move with it in this rotation, the inner malleolus backward and the outer malleolus forward. As the foot is supinated, there is a movement downward of the scaphoid over the head of the astragalus as well as a movement inward.

An important question may now be brought up in connection with this discussion. During the execution of flexion and extension in a seemingly simple ginglymoid diarthrosis like the ankle joint, what is the function of the fibula? Does it possess much elasticity; does it move, and if so, how and where?

We shall mention the opinions of several investigators, beginning with Humphry,³ who stated:

It is not enough to say that the socket of the leg bones is shaped in conformity with this configuration of the articular surface of the astragalus. For, if that had been all, and if the fibula had, like the inner malleolus, formed a part of the tibia so that the socket had been hollowed out of the solid bone and had maintained an unvarying size, it could not have been adapted to the astragalus in the different positions of the limb. It would have either been too large when the joint was *extended* or too small when it was *bent*. But the outer malleolus, being a little movable, permits a slight alternate widening and narrowing of the socket in flexion and extension; so that freedom of movement is combined with the maintenance of an exact coaptation of the articular surfaces. This yielding of the outer malleolus in a lateral direction, under the pressure of the articular surface of the astragalus during flexion, and its recoil in extension depend not so much upon a yielding of the ligaments that bind it to the tibia as upon the elasticity of the bone itself. Hence a careful examination will show that during flexion, when the malleolus is pressed outward, the shaft of the fibula is, at its narrowest part, just above the ankle, bent a little inwards; and vice versa, when the joint is extended, the shaft recoils to its former distance from the tibia.

Ashhurst⁵ stated that Nancrede called Humphry's theory "posterous and untrue." We cannot find any references about that remark. We believe that these are Ashhurst's own words. In the first place, Nancrede was not aware of the work and teaching by Miles and Humphry some twenty years before him. Nancrede⁶ merely answered an attack on him for plagiarism by Dr. Randolph Winslow. Dr. Winslow pointed out to him that all this was known and taught by others. However, Nancrede stated that a little reflection would demonstrate the mechanical impossibility of Humphry's view about the yielding of the external malleolus in a lateral direction during flexion and its recoil in extension.

Nancrede,⁷ in another article, went on to explain his views, for a part of which he justly claimed originality.

. . . all the ligamentous fibers pursue an *oblique course from the tibia downward to the fibula*, and that the capsule of the superior tibio-fibular joint is a loose one.

The diagram [fig. 5] will show the course pursued by the fibers . . . the apposed rough surfaces of the inferior tibio-fibular joint are connected by a short, felt-like collection of fibrous tissue—i. e., the inferior interosseous ligament.

. . . the ligaments must be perfectly inextensible and inelastic to perform their functions properly.

A little reflection will demonstrate that, in walking, the moment the foot is placed upon the ground the body still tends to go forward from its own impetus, and there is a marked tendency for the leg bones to slip forward upon the dorsum of the foot. This is not theory, but a demonstrable fact. Some provision against this must be made. If the immunity from displacement had to depend on the posterior ligament of the ankle-joint, it would have to be enormously strong. But let it never be so strong, unless it were *tight* it would not prevent luxation. If, however, it were tense in all positions where this forward displacement was liable to occur, it *would render flexion utterly impossible*. What, then, is the arrangement found? Simply that the astragalus is wedge-shaped, with its base in front, so that the more the leg bones tend to slip forward the tighter the articular surfaces are pressed together. This also is not theory, but a simple mechanical fact. The shape of the bony surface—excluding the muscles, which, as is too commonly overlooked, are often the most important ligaments of a joint—is absolutely the only obstacle worth mentioning to forward displacement of the leg bones. . . .

5. Ashhurst, A. P. C., and Bromer, R.: Classification and Mechanism of Fractures of the Leg Bones Involving the Ankle, Arch. Surg. 4:50-129 (Jan.) 1922.

6. Nancrede, C. B.: An Answer to Dr. Randolph Winslow's "Reply" to Dr. Nancrede's Paper upon the Tibio-Fibular and Ankle Joint, Maryland M. J. 7: 76-78, 1880.

7. Nancrede, C. B.: Some New Observations upon the Anatomy and Functions of the Ankle and Tibio-Fibular Joints, Philadelphia M. Times 10:316-318 (March 27) 1880.

This shape, however, of the astragalus and its socket, if the latter were rigid, would completely arrest flexion, as the broad anterior end, already firmly embraced by the malleolar arch, could not be made to pass backward into the still narrower portion of the socket, as is actually the case in flexion. . .

How, then, is an *adaptable* socket provided? Simply by having *two* bones in the leg, *one of which is movable*, the other fixed. By examining the diagrams it will be seen that the tibia and fibula can be compared to the two halves of a parallel ruler, and the ligamentous fibers to the two brass arms of the same instrument. Both the ligament and the brass arms are inextensible, but any wedge-like object insinuated between the two halves will push up the movable half and widen the space between them.

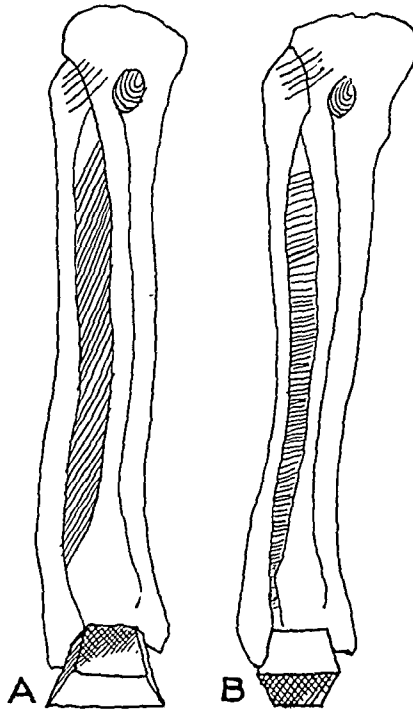


Fig. 5.—Direction of the fibers of the lower part of the interosseous membrane in extension (A) and flexion (B) of the foot.

Just so in the ankle-joint. In extreme extension [fig. 7] the narrow part of the astragalus is carried forward to that part of the socket which before accommodated the wide portion of that bone; and yet there is complete apposition of the bony surfaces, because the movable bone—i. e., the fibula—glides down. Again, in flexion the wide anterior portion of the astragalus is pressed between the narrower portion of the socket, which is widened by the fibula gliding *upward*. This upward gliding approximates the attachment and origin of the ligamentous fibers just enough to permit the two malleoli to be sprung apart sufficiently to admit the base of the astragaloid wedge. From the mode of attachment of the middle band of the external lateral ankle ligament—viz., in front and above the apex of the internal malleolus [he meant external malleolus]—this structure is tense in every position of the joint, and especially in extension winds around the malleolus, thus pulling it down and narrowing the socket in the extended position when such a condition of the malleolar arch is demanded.

From the foregoing statement it is apparent that Nancrede should claim originality for his views about the gliding upward and downward of the fibula.

NOTE.—In our brief communication on the structure and function of the ankle joint, the universally accepted views have been put forth as a matter of simplicity. These views are shared to a great extent by the original researches of von Meyer, Langer, Henke, Heuter, Meissner, Goodsir and others. Mr. W. Arbuthnot Lane, however, making an independent and exhaustive examination of the ankle joint in 1888, offered views on this subject, some of which differ materially from those mentioned in our review. The latter author called attention to the following facts:

(a) One must examine the astragalus in the recent state and not as a dry bone; one will then observe a "ligamentous facet" or "triangular area" as being cut off from the posterior and outer part of its upper surface; it is nonarticular; during flexion the posterior ligament, together with the posterior inferior tibiofibular and the posterior portion of the external lateral ligament, rests and plays on the triangular area.

(b) Also, during flexion of the ankle, the ligaments which are chiefly engaged in preventing the separation of the malleoli by the wedge-shaped internal articular surface of the astragalus are: the anterior inferior tibiofibular ligament, the posterior fasciculus of the external lateral ligament and the back part of the deltoid ligament. The interosseous membrane, the posterior inferior tibiofibular ligament and the inferior interosseous ligament take but a secondary share in this work.

(c) In complete extension of the ankle joint the concavity on the projection on the back of the astragalus comes into contact and articulates with the corresponding little articular surface on the tibia and with the adjacent portion of the posterior inferior tibiofibular ligament; the impact of these two opposing surfaces limits the movement of extension. In this position the only other articular surfaces in contact with each other are the outer articular surface of the talus with the corresponding facet on the outer malleolus.

(d) The transverse ligament is but a portion of the posterior ligament of the ankle joint. This posterior ligament is a distinct and important structure. It is attached externally to the fibula in the interval between the attachments of the posterior inferior tibiofibular ligament and the posterior fasciculus of the external lateral ligament. It consists of radiating fibers which cover in the ankle joint posteriorly. The upper margin of this ligament is practically continuous with the posterior inferior tibiofibular ligament and its lower limit with the posterior fasciculus of the external lateral ligament.

(e) The posterior fasciculus of the external lateral ligament limits and opposes movements both of complete flexion and of complete extension of the ankle joint, for the reason that its fibers occupy a horizontal plane and the interval between its points of attachment is least where the joint occupies a position midway between complete flexion and extension. Any deviation from this posture renders the fibers oblique.

(f) The same author maintained, therefore, that in any degree of flexion or extension of the ankle the head of the astragalus cannot be displaced inward owing to the strain exerted on it in an outward and backward direction by the anterior fasciculus of the external lateral ligament. It cannot be displaced outward on account of the strain

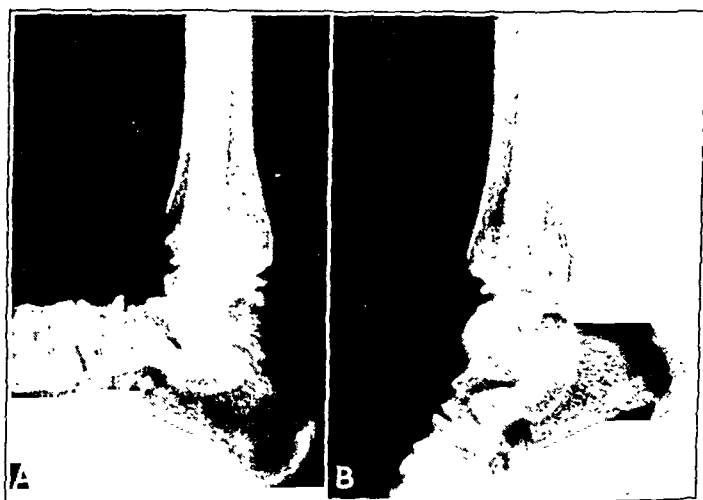


Fig. 6.—*A*, descent of the fibula in plantar flexion; *B*, ascent of the fibula in dorsiflexion.

exerted on it by the anterior portion of the deltoid ligament in a backward and inward direction.

REVIEW OF THE LITERATURE

In 1756 Sir Percival Pott suffered a compound fracture of both bones of the lower part of the leg, which resulted not only in his survival but in the repair of the fracture and later in 1768 in a description of "Pott's fracture." We refer the reader to this interesting and sparkling treatise in a compilation by Sir James Earle, "The Chirurgical Work of Sir Percival Pott, with Observations."⁸

We were not only regaled by this description but by the good judgment shown by Sir Percival when he refused to be transported from

8. Pott, Percival: *The Chirurgical Works of Percival Pott*, Philadelphia, J. Webster, 1819, pp. 246-252.

the site of the accident until the leg had been immobilized, a principle in treatment of fractures which is neglected by the modern surgeon and the attendant of the police ambulance.

Pott, in his treatise, pointed out the power which the peroneus muscles acquire in consequence of the loss of support occasioned by fracture of the fibula and the resulting eversion and elevation of the foot.

Preceding and following Pott up to the time of Sir Astley Cooper⁹ and Dupuytren¹⁰ were several interesting writers, among whom we may mention Petit¹¹ (1723), Bromfield¹² (1773), Pouteau¹³ (1783), Castella¹⁴ (1808) and Bell¹⁵ (1809).

Cooper⁹ (1830-1840) seems to have had an appreciation of the various dislocations, including posterior displacement, which occurs in posterior marginal fracture.

Dupuytren¹⁰ (1830-1840), in a masterful treatise on "Fractures of the Fibula", in which he reported 207 cases with 5 deaths, specially pointed out the ligament tears, the result and the fact that dislocation of the foot at the ankle joint does not occur without fracture.

We now come to Maisonneuve¹⁶ (1840), who described lateral dislocation of the foot with high fibular fracture, now known as the Maisonneuve fracture, and presented an interesting discussion on the mechanism of injuries to the ankle. He was first to point out the importance of the tibiofibular diastasis which we are emphasizing in this paper.

In 1879 Tillaux¹⁷ discussed fractures of the ankle, and the so-called "third fragment" was introduced.

9. Cooper, A. P.: *A Treatise on Dislocations and Fractures of the Joints*, edited by B. B. Cooper, Philadelphia, Blanchard & Lea, 1851, pp. 246-298.

10. Dupuytren, Gillaume: *On the Injuries and Diseases of Bones*, translated and edited by F. le Gros Clark, London, New Sydenham Society, 1847, pp. 234-315.

11. Petit, Jean-Louis: *Traité des os: Dans lequel on a représenté les appareils et les machines qui conviennent à leur guérison*, Paris, C.-E. Hochereau, 1723.

12. Bromfield, W.: *Chirurgical Observation and Cases*, London, T. Cadell, 1773.

13. Pouteau, Claude: *Oeuvres posthumes*, Paris, P.-D. Pierres, 1783.

14. Castella, M.: *Essai sur les fractures du péroné*, Landshut, J. Thomann, 1808.

15. Bell, Charles: *A System of Operative Surgery, Founded on the Basis of Anatomy*, ed. 2, London, Longman [and others], 1814, pp. 363-365.

16. Maisonneuve, J. G.: *Recherches sur la fracture du péroné*. Arch. gén. de méd. 1:165-187 and 433-473, 1840.

17. Tillaux, Paul: *Traité d'anatomie topographique avec applications à la chirurgie*, Paris, Asselin & Houzeau, 1879.

Hoenigschmied¹⁸ in 1877 made some exceedingly interesting studies, 125 in all, on cadavers to determine the mechanism of fracture of the ankle.

Bondet in 1899 and Destot¹⁹ in 1911 introduced physiologic classifications, adopted later by Quenu²⁰ and Tanton, both of whom used these classifications and added to theories in mechanism.

The mechanism of Pott's fracture was one of the favorite discussions in the clinics of Dr. John B. Murphy.²¹ One of us remembers with what emphasis Dr. Murphy described the mechanism. He also recognized the importance of diastasis but denied the possibility of Pott's fracture occurring by inversion of the foot.

The advent of the x-rays has greatly enhanced our knowledge of the many combinations of fragments, of the dislocations and especially of the posterior marginal fragment and the arthritic changes which follow these fractures.

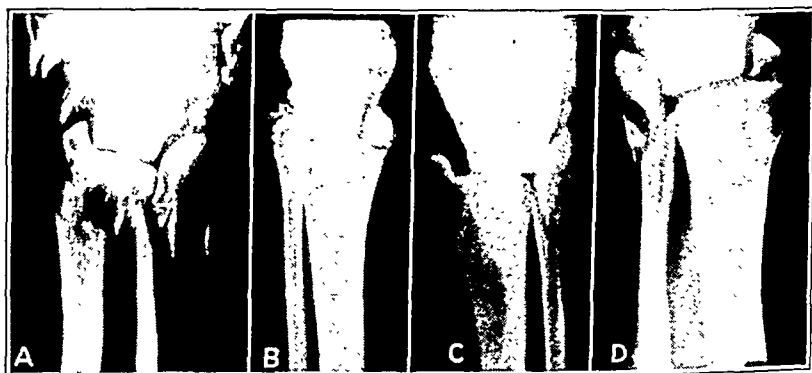


Fig. 7.—A, compression fracture; B, bimalleolar fracture; C, simple Pott's fracture without fracture of the internal malleolus, and D, simple Pott's fracture with an oblique fracture of the fibula above the malleolus and the internal malleolus—the common type.

Among the outstanding American writers are Kellogg Speed,²² who published a report based on a study of 208 cases of Pott's fracture from the Cook County Hospital, and Ashhurst and Bromer,⁵ who

18. Hoenigschmied, J.: Experimente über die Zerreibungen der Bänder im Sprunggelenk, *Deutsche Ztschr. f. Chir.* 8:239-260, 1877.

19. Destot, Etienne: Fractures de la région malléolaire, in *Traumatismes du pied et rayons X*, 1911, pp. 75-134.

20. Quenu, E.: Plaies de pied et du cou-de pied par projectiles de guerre, Paris, F. Alcan, 1918, pp. 185-190.

21. Murphy, J. B.: Pott's Fracture, *Surg. Clin.* 1:451, 1912; Ancient Pott's Fracture: Operative Reduction; Nailing of Malleoli, *ibid.* 5:349, 1916.

22. Speed, Kellogg: A Discussion of Pott's Fracture with Complications, Based on a Series of Two Hundred Eight Cases, *Surg., Gynec. & Obst.* 19:873-882, 1914.

reported 300 cases of fractures of the ankle, giving, perhaps, the most detailed classification with an interesting study of the literature.

The works of Cotton and Berg,²³ especially on posterior marginal fractures and on a classification according to dislocation, are important landmarks in the development of this subject.

We are also much interested in the fact that Bardenheuer advocated traction in the treatment twenty years ago, a fact which is now generally accepted by the German surgeons, especially Felsenreich²⁴ and L. Böhler, in the more serious types of fractures of the ankle.

Other interesting contributions have been made by Stimson, Stevens,²⁵ Shands,²⁶ Delbet, Robert,²⁷ Hubmann²⁸ and Pels-Leusden.

MECHANISM OF FRACTURES OF THE ANKLE

In considering the mechanism of the ankle joint, one notices that the column transmitting the weight of the body from the thigh to the foot consists of two bones, which are so united as to form a solid medium, the fibula gliding to a slight extent upward and downward during dorsiflexion and plantar flexion, respectively, allowing no lateral motion. The base of the column is the foot, but the ankle joint is not placed in the center of the weight-bearing arch of the foot. If a vertical line is dropped from the center of the base of the femur, it falls on the inner part of the astragalus, which is itself placed at the inner and posterior part of the foot. This accounts for the greater power of the adductor or supinator muscles. This line again divides the foot as regards its anteroposterior axis into two unequal portions, nearly three-quarters being in front of and one-fourth behind the center of gravity. It is well known, as pointed out by Osgood, that in the uninjured and healthy limb the adductor or supinator muscles exceed the pronator muscles in strength in the proportion of 5:4. But as soon as fracture of one of the bones of the lower part of the leg is produced, the ratio does

23. Cotton, F. J., and Berg, R.: Ankle Fractures: New Classification and New Class, *New England J. Med.* **201**:753-760 (Oct. 17) 1929.

24. Felsenreich, Fritz: Untersuchungen über die Pathologie des sogenannten Volkmannschen Dreiecks neben Richtlinien moderner Behandlung schwerer Luxationsfrakturen des oberen Sprunggelenks, *Arch. f. orthop. u. Unfall-Chir.* **29**:491-529, 1931.

25. Stevens, James. H.: Compression Leverage Fractures of Ankle Joint, *Surg., Gynec. & Obst.* **38**:234-252, 1924.

26. Shands, A. R.: Fracture-Dislocations of the Ankle: Analysis of Series of One Hundred Nine Cases, *Internat. J. Med. & Surg.* **42**:238-244, 1929.

27. Robert, Leslie: Treatment of Ankle and Leg Fractures by the "Delbet" Ambulatory Plaster Splint, *Brit. J. Surg.* **15**:414-429, 1928.

28. Hubmann, Paul: Ueber die Frakturen des obern Sprunggelenks mit besonderer Berücksichtigung der hinteren Luxationsfraktur und ihrer Behandlung, *Beitr. z. klin. Chir.* **147**:417-433, 1929.

not hold any more. The long and short peroneus muscles, assisted by some of the muscles lying in front of the ankle (the extensor digitorum longus and peroneus tertius), overcome the power of the adductor or supinator muscles and therefore evert the foot and help to produce a lateral dislocation.

For this reason we must forget previous conceptions that all Pott's fractures are produced by turning the foot outward and that turning the foot inward produces, when fracture occurs, always a medial dislocation.

Clinical experience is of no assistance, since most patients cannot remember whether they turned the foot outward or inward.

For this reason any classification on an etiologic basis is untenable; nor does the dislocation reveal the mechanism.

Some authors explain the mechanism entirely along mechanical lines, having in mind the weight-bearing axis, various levers, stress

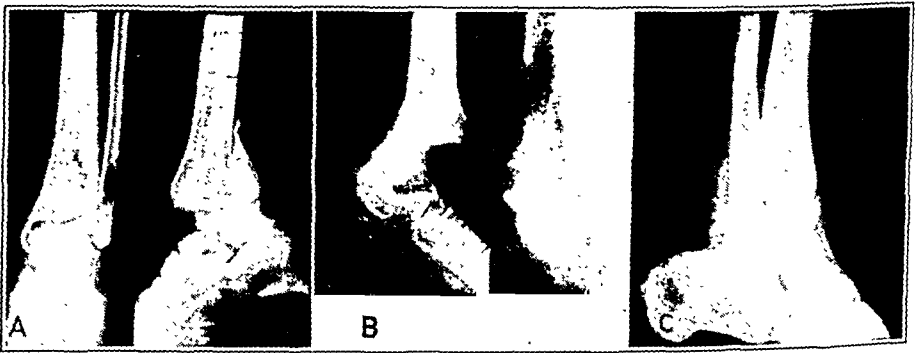


Fig. 8.—A, Pott's fracture with posterior marginal and posterior dislocation (a Cotton fracture); B, Pott's fracture with marked posterior dislocation but no posterior marginal fragment, and C, Pott's fracture with anterior chip (a Tillaux fragment).

and strain. Under "Anatomy and Physiology of the Ankle Joint" we have shown that the movement of the foot is not in a direct antero-posterior plane but in a plane inclined outward and obliquely, owing to the outward inclination of the toes, to the slight twisting of the tibial shaft and to the posterior position of the external malleolus. This, plus other factors, such as the varying equinus position of the foot (females), genu valgum or varum, the weight of the body, the type of the shoe, the grade of the terrain and other extrinsic forces, all bring forth various factors in the mechanism of production, and, after all, interest us in the mechanism of this fracture more from an anatomic standpoint.

Most writers in describing Pott's, or pronation, fracture have held the view that one of two lesions occur primarily. Stimson, Bonnet and Tillaux stated that the first lesion is the tear of the internal lateral

ligament or the internal malleolus, which allows the tibia to move laterally and later to act as a fulcrum in fracturing the fibula. Murphy, Speed, Ashhurst and Maisonneuve stated that the astragalus in eversion of the foot acts as a fulcrum, first fracturing the fibula, and that the anterior inferior tibiofibular and the internal lateral ligament tear later in Pott's fracture.²⁵

Maisonneuve in 1840 was the first to appreciate the rôle played by the inferior tibiofibular ligaments in the production of fractures of the ankle. Other writers have referred to the diastasis and the disability resulting therefrom.

Examination of leverage injuries of the ankle joint, whether sprain or Pott's fracture, invariably shows local tenderness slightly medial and inferior to the external malleolus, pointing to a lesion of the anterior inferior tibiofibular ligament (Aitken, 1934).

The collateral ligaments are the strongest ligaments of the ankle joint. The inferior tibiofibular ligaments, although resistant to force, are subject to constant strain in any position of the foot. This strain is accentuated by the up and down movement of the distal end of the fibula during flexion and extension. This fact, brought out in our anatomic discussion, has been previously overlooked to a great extent.

Measurements made after fracture-dislocations of the ankle joint show commonly a widening in the mortise due to diastasis of the tibiofibular articulation. Reference to our "Analysis of Data" shows this condition present grossly in 40 per cent of the roentgenograms. It is difficult, unless comparative roentgenograms are made, to determine a little diastasis.

The foregoing anatomic and clinical facts lead us to believe that the tear in the anterior inferior tibiofibular ligament with subsequent diastasis is not only a constant lesion in leverage injuries of the ankle joint, including sprains, Pott's fracture and other types of fracture, but that it is the primary lesion.

We know of no permanent way of proving our observations but feel that our views are fairly well founded on an anatomicopathologic basis, whereas the opinions of previous writers are only theories visualized on mechanical grounds.

In more severe violence the posterior inferior tibiofibular ligament and even the interosseous ligament may be torn, causing more marked diastasis.

After a tear in the tibiofibular ligament, it acts as a fulcrum, the degree of tear determining the site of fracture in the fibula. With a tear in the interosseous ligament, the fracture is high on the fibula, as described by Maisonneuve.

The tear in the anterior inferior tibiofibular ligament is followed by a tear in the internal lateral ligament, and this, together with the

up and down movement of the fibula, allows a rotary movement of the astragalus. This accounts for the large percentage of oblique fractures (153 in 300 roentgenograms).

As before stated, Pott's fracture can occur with both supination or pronation of the foot at the time of accident. When pronation does not result after supination, there is a medial dislocation with a vertical or an oblique fracture in the tibia or in the internal malleolus.

A bimalleolar fracture is usually caused by supination or pronation but may be also caused by a fall forward or backward, with the foot either in plantar flexion or in dorsiflexion. The latter mechanism also accounts for a solitary anterior or posterior marginal fracture, in some of which we find a tear in the anterior or posterior tibiofibular ligament with diastasis.



Fig. 9.—*A*, Pott's fracture with a posterior chip (a Tillaux fragment)—low oblique fracture of the fibula; *B*, Maisonneuve's type of Pott's fracture—a high fracture of the fibula, and *C*, simple Pott's fracture, with fracture of the internal malleolus—low subperiosteal fracture in the external malleolus.

A marginal fracture usually occurs as a complication of pronation, supination or bimalleolar fracture. The posterior lip is more often involved because of its greater posterior declination. A posterior marginal fracture is more commonly seen in females than males, which leads us to believe that the equinus position of the foot allows greater rotation and backward displacement of the foot.

CLASSIFICATION

A study of 378 roentgenograms of fractured ankles makes us wonder why a classification should be made at all. It seems more natural to report each individual case according to the roentgenographic picture.

On the other hand, some classification which is simple must be used for teaching purposes. Our conception of these injuries does not permit a classification merely on the type of dislocation, since there are tears in the ligament and various combinations of fragments, nor can we consider one on an etiologic basis such as suggested in the excellent monograph by Ashhurst and Bromer.⁵

Regardless of any objection to placing a colleague's name in the classification, one must agree that for years English-speaking people have called the pronation fracture of the ankle joint Pott's fracture. There may be no Pott's fracture, but for the sake of precedent and usage from now on we shall classify all fractures of the lower part of the fibula with lateral dislocation of the foot as Pott's fracture; the reverse, as supination fracture. When there is no dislocation, one has simple or bimalleolar fracture. A compression fracture refers to upward dislocation of the astragalus with comminution of the lower end of the tibia and the fibula.

Should there be a small anterior or posterior lip (a Tillaux fragment) or an anterior or posterior marginal fragment (figs. 9 *B* and *C* and 10 *A*), this condition is considered as a complication. Solitary marginal fracture is rare. Thus we may refer to Pott's fracture with a posterior fragment or a bimalleolar fracture with an anterior Tillaux fragment.

This classification takes into consideration that lesions of the ankle consist of tears in the ligament, dislocations and fractures and quickly suggests to the student both the pathologic process and the treatment required.

TREATMENT OF INJURIES TO THE ANKLE

The main objects in treating injuries of the ankle joint are as follows: (1) to reduce the dislocation, (2) to reduce the fracture, (3) to reduce the tibiofibular diastasis, (4) to maintain a reduction until ligamentous and bony repair has been obtained, (5) to protect the vascular system during the repair and (6) to restore function.

As a temporary measure, in all cases of simple injuries of the ankle we apply a posterior molded splint lined with sheet wadding. This is often done at home to protect the injury and make the trip to the x-ray laboratory or hospital more convenient to the patient. After the patient is hospitalized all compound fractures are surgically cleaned by débridement. No internal suturing is done, and the skin is closed without drainage. Fractures are immediately reduced, and a posterior molded splint is applied. If the wound is extensive and is so placed that the cast might produce pressure, the fracture-dislocation

is treated by means of a Kirschner wire or a Steinmann pin through the os calcis, extension being best obtained with the knee bent on a Braun or Böhler splint.

It is important to ascertain whether the fracture-dislocation has occurred in the usual manner or whether there has been additional direct trauma, such as the limb's being run over by a car wheel, or any other form of contusion, since in such accidents the patient must be informed

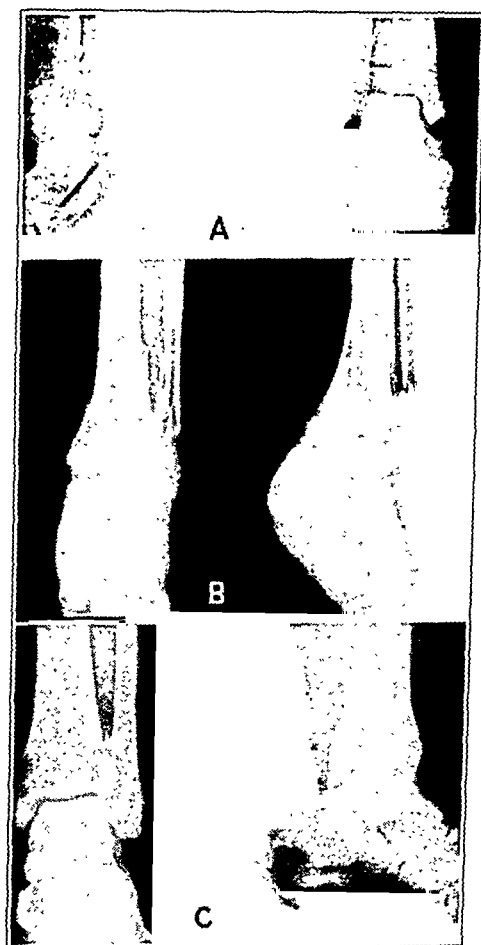


Fig. 10.—*A*, epiphyseal separation with a posterior marginal fracture running into the epiphyseal line; *B*, supination fracture, and *C*, simple fracture of the external malleolus.

of the likelihood of blebs, gangrene or sloughs, lest he later blame the surgeon's splint.

In simple fractures without dislocation or displacement an anesthetic may not be necessary since the limb can be immobilized with the usual posterior molded splint. If, however, there is considerable tenderness over the anterior inferior tibiofibular ligament or should the roentgenogram show a distinct diastasis, we even then use a local or general anesthetic in order to apply the redresseur.

Reduction.—This is done as soon as diagnosis is made by means of a roentgenogram. Should there be a swelling, the limb is elevated for twenty-four hours, and effleurage is used to reduce the edema.

The reduction should be done with the patient under an anesthetic, either local or general, preferably ether or ethylene. In all cases of Pott's fracture reduction is performed with the leg flexed at right angles, dorsiflexion and adduction of the heel being used, and for supination fracture-dislocations the reverse of this procedure is

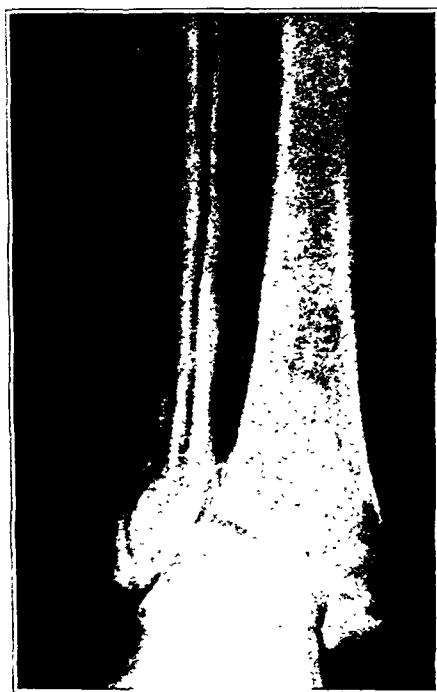


Fig. 11.—Pott's fracture with posterior marginal fracture, showing marked diastasis, suggesting also involvement of interosseous ligament.

employed—with either type of fracture, the foot being held in mid-position.

All posterior dislocations with posterior marginal fragments are reduced with cautious dorsiflexion (see maintenance of reduction).

The internal malleolus, when fractured and displaced, is pushed upward with the palm of the hand.

Bimalleolar fracture is treated in midposition with right angle dorsiflexion.

It is the purpose of this paper to add one additional procedure in the reduction of Pott's fracture; that is to reduce the diastasis by

means of a redresseur to the lower part of the tibia and fibula above the malleoli. The instrument is applied for from three to five minutes, the compression being removed just before the unpadded posterior molded splint of plaster is applied. Not alone is the diastasis overcome, but a better mortise and position of fragments are effected in a bimalleolar fracture. Neglect to reduce the diastasis results in abnormal lateral motion, pes valgus, shortening of the tendo Achillis, faulty weight bearing and later arthritic change.

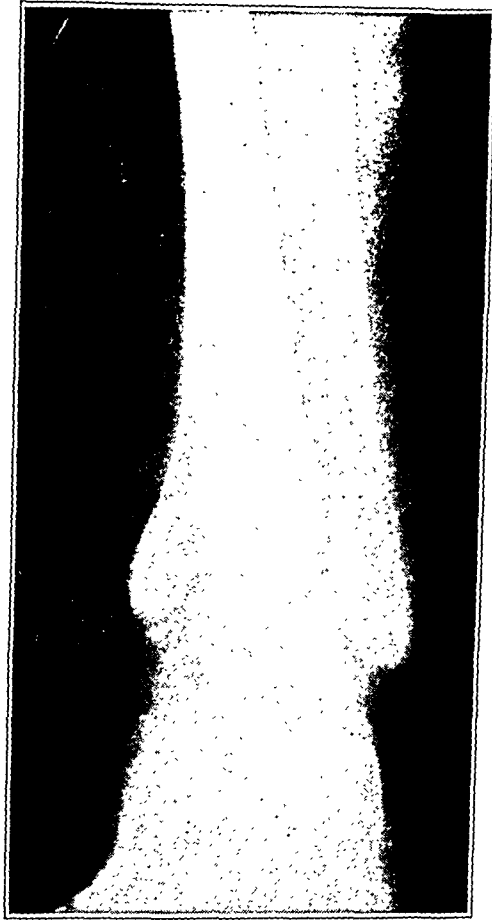


Fig. 12.—Simple Pott's fracture. The fibula is fractured at a still higher level.

When diastasis is marked and second roentgenograms still show separation, we apply extension by the Kirschner wire, which puts the collateral ligaments on stretch, thereby bringing the tibia and the fibula together. We here caution against overextension (fig. 14).

A common error is to put a supination fracture with medial dislocation in adduction. This only increases the dislocation.

When a posterior marginal fragment complicates fracture, caution should be used not to put the foot in too much dorsiflexion.

A compression fracture is treated as a routine with Kirschner wire through the os calcis. The reduction of dislocation can be obtained by adjusting the bow of the Kirschner apparatus. The redresseur is usually used later for this type of fracture because of the greater tendency to edema and blebs.

Maintenance of Reduction.—It is easy to reduce Pott's fracture even when complicated by a marginal fragment, but is difficult to

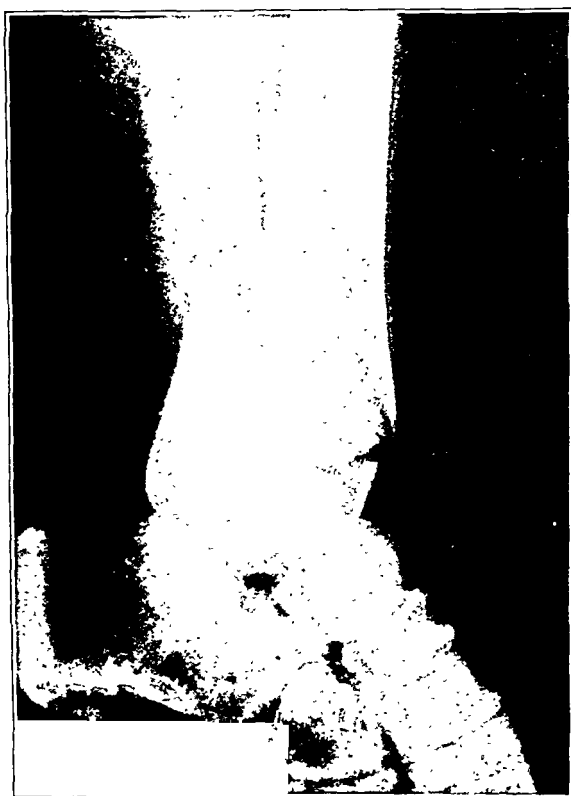


Fig. 13.—Pott's fracture with anterior and posterior marginal fractures.

maintain the reduction, because the diastasis predisposes to redislocation of the astragalus. Formerly, many poor results could be attributed to the circular cast padded with so much cotton that the reductions were lost in the shrinkage of the plaster.

The ordinary type of Pott's fracture can be best immobilized in a posterior molded splint without padding. This splint is applied immediately after the redresseur has been removed and extends from the middle of the thigh to beyond the toes. A walking iron can be applied several days later in cases of the more simple types of fracture by

means of circular plaster above the malleolus and above the knee. Our statistics show that the average immobilization is about five weeks in a case of simple Pott's fracture and much longer when there is a posterior marginal fragment. In the latter cases one may not be able to maintain reduction in the ordinary plaster splint, and under such circumstances we advise using a pin or a Kirschner wire extension on a Böhler splint for five weeks. We advocate that extension be used more



Fig. 14.—Overextension and deformity caused by improper traction.

often in cases of the severe types of fractures of the ankle to reduce the diastasis, to prevent redislocation and to keep the posterior fragment pulled down.

Roentgenograms are made immediately after the reduction, and in cases of anterior or posterior marginal fragments they are made every seven days until union is assured.

In many cases a boot made of a paste of zinc oxide ²⁹ is desirable during the next few weeks to support the circulation. Weight

29. The composition of this zinc oxide paste by weight is as follows: 1 part of chemically pure zinc oxide, 2 parts of good gelatin, 3 parts of water and 4 parts of chemically pure glycerin.

bearing varies with the amount of swelling and union. The average weight bearing in simple Pott's fracture is eight weeks. We advise against weight bearing in a case of Cotton fracture for a period of from twelve to fourteen weeks.

Restoration of Function.—Passive motion is entirely omitted from our treatment. Active motion can be obtained even with a boot of a paste of zinc oxide. When the boot is not used, we find our best results in restoring function to be derived from the use of baking, Swedish massage and hot and cold foot baths.

The only additional treatment which we employ is the application of the redresseur in reducing tibiofibular diastasis, which is present in all injuries to the ankle, and to advocate a greater use of extension (traction) to prevent disabilities.

SUMMARY

In our report, supplemented by a morphologic and physiologic study and a clinical study of the pathologic picture of fractures of the ankle, we have emphasized the following points:

1. The primary lesion in leverage fractures of the ankle joint is the tear in the anterior inferior tibiofibial ligament, followed by a certain amount of diastasis.
2. The height of the fibular fracture depends on the degree of diastasis plus the gliding of the fibula in dorsiflexion and plantar flexion (already described).
3. The diastasis in the inferior tibiofibular articulation is the cause of much disability, faulty weight bearing and arthritic changes and should be prevented at the time of injury by applying a redresseur or even traction with a Kirschner wire at the time of reduction and immobilization.
4. All abduction fractures of the ankle joint should be called Pott's fracture. We have given a simple classification, including all other types of fracture and their complications.

RETROPERITONEAL TERATOMA

P. M. MECRAY JR., M.D.

AND

W. D. FRAZIER, M.D.

PHILADELPHIA

The literature on the pathologic structure of the teratoma is in a most unsatisfactory state. On a recent occasion three pathologists were questioned as to the elements necessarily present in a tumor to admit it to classification as a teratoma. Each presented different criteria. The literature reveals a similar divergence of opinion, and the confusion is evidenced further by the number of theories that have been advanced by authors to explain the origin of such a tumor. To enter into a discussion of these subjects is beyond the scope of this paper, but the studies presented here strongly suggest that a teratoma arises as a misplaced blastomere. The more nearly totipotent the cell, the more differentiated will be the tumor when it grows.

Recognizing fully the objections to this theory, we believe that it still remains the most logical explanation of parasitic monsters and teratomas. By following this reasoning, teratomas may be subdivided into two types: the true teratoma and the teratoid tumor. The former, containing the analog of one or more organs, is derived from a more nearly totipotent blastomere than the latter, which is unable to produce any formed organ, even though it, too, contains representatives of all the embryonal elements. The transition between these artificial classes is so gradual that the classification accorded any borderline tumor depends on the pathologist. In reviewing the literature listed in the bibliography, we have attempted to ascertain from the description of the tumor whether or not formed organs were present, and our review has revealed thirty-six cases of retroperitoneal teratoma. The data in these cases, with the exception of those in the cases presented by Karvonen and Cahill, reports of which were not available, are recorded in the accompanying table. In addition we desire to present a new case which we have observed.

REPORT OF A CASE

P. S., a 29 year old man, was admitted to the surgical service of Dr. I. S. Ravdin in the Hospital of the University of Pennsylvania on Sept. 9, 1935, with a chief complaint of pain in the right side of the abdomen. He stated that his

From the Surgical Clinic and the Laboratory of Surgical Pathology, Hospital of the University of Pennsylvania, and the Harrison Department of Surgical Research.

Data on Cases of Retroperitoneal Teratoma and Teratoid Tumor Reported in the Literature up to 1936

Author	Sex	Age*	Location of Tumor	Size	Manner of Obtaining Specimen	Result of Operation	Formed Organs Present	Symptoms
Ballasov.....	F	21	M	Operation	Death	Yes
Bauer.....	M	14	Left	L	Operation	Death	No
Brouha.....	F	26	Right	S	Autopsy	No	Mass
Pickinson.....	F	2	Right	M	Autopsy	Yes
Dugarte and David.....	M	Neonatal	Lumbar	S	Autopsy	No	Mass
Feldmann.....	F	20	R. U. Q.	L	Operation	Recovery	No	"Pressure symptoms"
Gordon.....	F	50	R. U. Q.	S	Operation	Recovery	Yes	Mass
Gross.....	F	26	R. U. Q.	M	Operation	Death	Yes	Mass
Gude.....	F	9	R. U. Q.	L	Autopsy	Yes	Mass
Hosmer.....	F	8 mo.	Right	M	Operation	Yes
Iru.....	F	9 mo.	Left	M	Operation	Death 8 mo. later	Yes	Mass
Johnson and Lawrence.....	M	33 mo.	Left	S	Exploration	Yes
Kupko.....	M	10 mo.	L. U. Q.	M	Autopsy	Yes	Mass; ecchexia
Kolb.....	F	7 wk.	Left	S	Autopsy	Yes	Mass; ecchexia
Kostich.....	M	22	L. U. Q.	L	Operation	Death	Yes	Mass; pain
Kuznetsov.....	M	..	Left	L	Exploration	No	Mass; ecchexia; constipation
Landliver and Ipatruguliro.....	M	45	L. U. Q.	M	Operation	Recovery	Yes	Pain
Lexer.....	F	11	L. U. Q.	..	Operation (twice)	Recovery	No	Fever; pain; mass
Lightwood.....	..	9 wk.	R. U. Q.	S	Autopsy	No
Marchand.....	F	35	L. U. Q.	S	Operation	Death	No	Mass
Maydl.....	F	..	L. U. Q.	..	Operation	Yes
Meckel.....	Autopsy	No
Nicholson, C. M.....	M	25	R. U. Q.	S	Exploration	Death	Yes	Mass; vomiting; pain
Nicholson, G. W. P.....	F	4 mo.	L. U. Q.	S	Autopsy	Yes	Mass
Pillet.....	F	21	Lower	L	Biopsy	Death	Mass
Portugal.....	F	17	L. U. Q.	S	Operation	Death	Yes	Mass; vomiting; pain
Roux.....	F	25	Unilateral	L	Autopsy	No	Mass; uremia
Ruge.....	M	27	Left	L	Operation	Yes
Seki.....	M	22 mo.	Left	M	Autopsy	Yes	Mass; pain
Shenolzer.....	M	2	Epigastrium	M	Autopsy	Yes	Mass
Terasako.....	F	3 mo.	R. U. Q.	S	Operation	Death	No	Mass
Tilmanx.....	F	22	L. U. Q.	M	Operation	Death	No	Rapid growth
Tsuda.....	M	17 mo.	Left	L	Operation	Death
Usundzaga and Mayor.....	F	28	L. U. Q.	S	Operation	Recovery	No	Pain
Watanabe.....	M	23	L. U. Q.	S	Autopsy	Mass

* Figures indicate years when not otherwise specified.

† Malignant.

health had been perfect until ten days before admission. Then, for the first time, he had noticed a dull pain in the right lower quadrant of the abdomen. This pain caused him to stop his regular work in a hosiery mill. A local physician examined him "thoroughly" and ordered him to bed. At no time did he have nausea, emesis or pyrexia. After two days of rest in bed the pain disappeared completely. On September 5, following the advice of his physician, the patient took a bottle of solution of magnesium citrate to relieve obstipation of six days' duration. This was effective, and after the passage there was noted for the first time a large nontender lump in the right upper quadrant of the abdomen. The mass persisted without change until his admission on September 9. Two days before, while walking, the patient was suddenly seized with knifelike pains in the right upper quadrant of the abdomen. These were excruciating for from five to six hours but after that gradually lessened in intensity until the time of his arrival at the hospital. Still there was no nausea, vomiting or fever.

His past medical history was essentially irrelevant, except that he had noted increasing constipation for the preceding two years. His family and social histories were not enlightening.

On physical examination, the patient was found to be well developed and to present no essential abnormality, save for the condition in his abdomen. In this region there was slight generalized tenderness, but no muscular spasm. In the right upper quadrant, nearer the umbilicus than the costal margin, a firm, smooth mass was felt, which on palpation seemed to be about the size of a lemon. It was well circumscribed and apparently did not extend toward the right costal margin. It was fixed, though it moved slightly with respiration, and was tender only to firm pressure. No other masses or organs were palpable.

Laboratory studies of significance showed a leukocyte count of 17,400 and a slightly accelerated sedimentation time. A roentgenogram taken after an enema of barium sulfate revealed the transverse colon displaced downward by a mass located in the right upper quadrant, which mass lay superior and posterior to the transverse colon but had no connection with it.

After two days' hospitalization a laparotomy was performed by Dr. I. S. Ravdin on September 11. Through an upper right rectus incision, the tumor was found to be lying retroperitoneally just below the liver, on top of the vena cava and lateral to the descending portion of the duodenum. Across its lateral surface ran the right ureter, and across the medial surface, the superior mesenteric vessels. It was covered by the transverse mesocolon, and when this had been divided the mass was found to be well encapsulated. The pseudocapsule or peritoneum was incised, and the tumor was carefully shelled out, with little bleeding. The posterior pole was firmly adherent to the vena cava. The raw surface was peritonized, and the abdomen was closed without drainage.

The patient's course after operation was uneventful. The incision was completely healed at the time of his discharge, on the sixteenth postoperative day. He returned two months later. At that time he felt entirely well, had gained weight and was completely relieved of his constipation. The wound was well healed and showed no evidence of weakness. No recurrent mass could be palpated. A series of high voltage roentgen treatments was given at that time. It was divided so that 50 roentgens was delivered through each of four portals covering the entire abdomen and the lower part of the thorax, and a second portion, consisting of 3,200 roentgens, was directed to the tumor bed.

Six months after his discharge the patient was readmitted to the hospital, because of a different complaint (headache). The opportunity was taken to study him at this time. Physical examination, a urogram and roentgen examina-

tion, after a barium enema, revealed no abnormalities in the retroperitoneal area. He had no symptoms referable to this region. The testicles were normal in size, shape and position.

He returned to the hospital in July 1936, with a painful swelling in the right side of his scrotum. This had developed rapidly, following an injury two weeks before. Examination revealed that the lesion was not traumatic or due to infection but was a neoplastic enlargement of the right testicle. The testicle was somewhat larger than a hen's egg and was firm, smooth and slightly tender and surrounded by a small amount of fluid. The patient's general condition was good, and he had lost no weight. General physical examination gave negative results. Orchidectomy was performed, and on microscopic examination typical teratomatous tissue was found, which we believe was the result of metastasis from his original tumor.

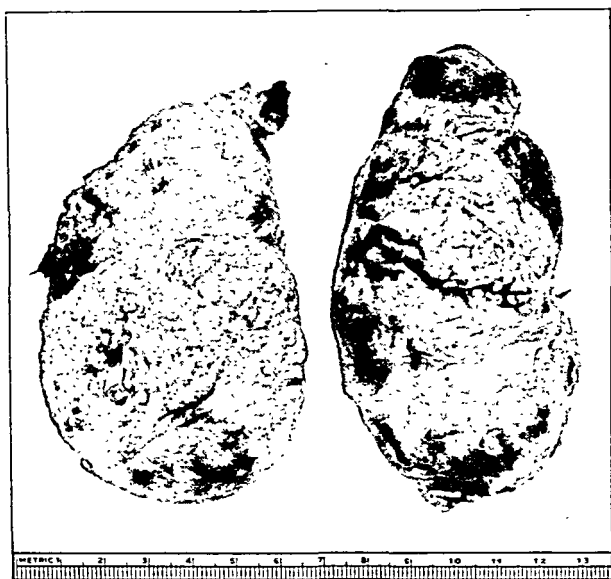


Fig. 1.—Outer view of the tumor, showing the nodular appearance. The site of attachment is at the top of the picture.

His fourth admission was only ten days later, and at this time he complained of a constant, dull, dragging pain in the right lower quadrant of the abdomen. There were no associated urinary or gastro-intestinal symptoms other than some increase in constipation.

Examination revealed a large firm, fixed mass just below the scar of the original operation and a smaller lesion farther down in the right lower quadrant. These had not been palpated at the time of the previous admission. Roentgen studies of chest, loins, spine and pelvis gave negative results, but the right iliopsoas muscle was partially obscured, apparently by the overlying tumor. These lesions seemed to be extensions of the original lesion. They were hard and fixed. We did not believe that they could be removed by operation. Roentgen therapy was begun immediately, and over a period of three weeks the patient received a total of 4,450 roentgens through six portals, covering the chest,

abdomen and pelvis. During this time his pain was completely relieved, and the palpable masses decreased considerably in size. He was told to return for further irradiation after six weeks' rest.

Pathologic Report.—Grossly the tumor was the size and shape of a large pear. It measured 10 by 6 by 5 cm. and weighed 155 Gm. The surface was covered with a glistening capsule, save for an area 3 cm. in diameter, which was the apparent site of attachment. Its surface was irregular and nodular (fig. 1). These whitish yellow nodules measured from 1 mm. to 1.25 cm. in diameter. To palpation they felt firmer than the supporting tissues. On section the tumor was found to be made up of myriads of small cysts (fig. 2), the great majority of which were filled with a sebaceous material. There was a second group of apparently thinner-walled cysts which contained a clear serous fluid. A third, less common class was observed, which contained both clear serous fluid and sebaceous material.



Fig. 2.—Inner view of the tumor, showing cystic structure. The areas of hemorrhage may be seen plainly.

The last two types of cyst were found, in the main, near the posterior attachment of the tumor. In the same area were several fairly well organized hemorrhages, the largest of which measured 3 by 3 by 1.5 cm. No formed organs were seen grossly.

Microscopically the tumor showed wide structural variations. Predominating were structures of mesoblastic origin. Among these, in order of frequency, were encountered spindle cells and connective tissue, moderate-sized, localized areas of angiomatous tissue, small areas of adipose tissue and one small plaque of cartilage. There was no evidence of the presence of muscle or bone.

Tissue of hypoblastic origin was least frequently seen. Several areas showed columnar epithelium bearing goblet cells. These were arranged in a manner resembling the glandular formation of the large intestine. The apparent secretion of these cells took the eosin stain. Occasional cysts were lined with epithelium of

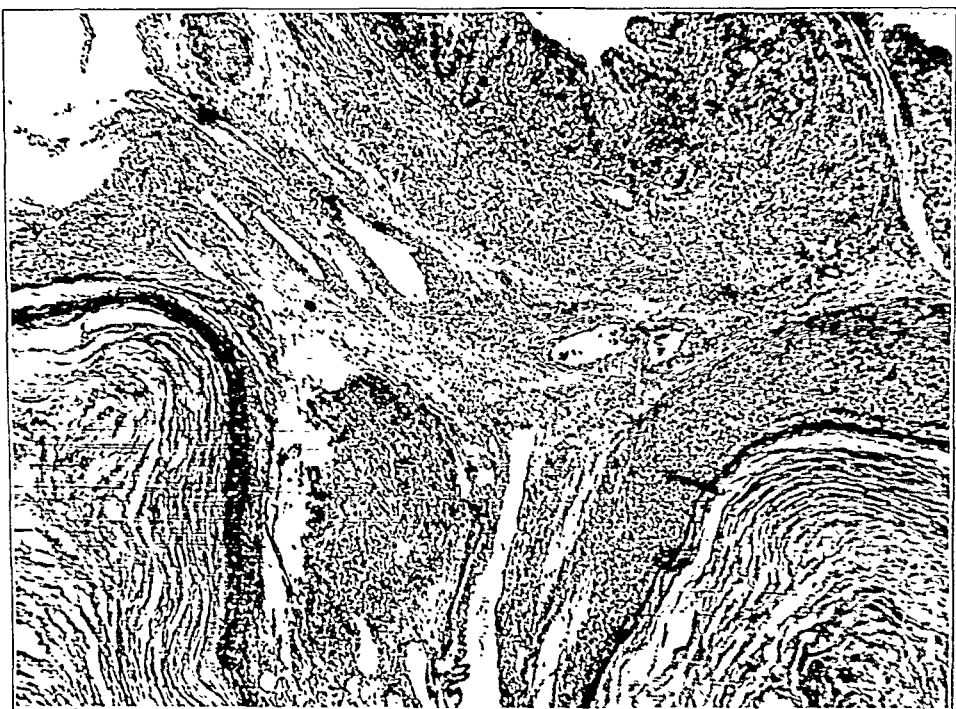


Fig. 3.—Photomicrograph showing three of the many cysts found in the tumor. The upper one is lined with goblet cells, and the lower two are lined with endothelial cells and filled with a colloid substance.



Fig. 4.—Photomicrograph showing a cyst lined with three different kinds of epithelium.

a pure columnar variety and others with a pure transitional type. In the latter class several papillary projections were observed. No cilia were demonstrated.

Epiblastic tissue was manifested by epidermoid cysts. These did not have hair, sweat glands or papillae, and it was impossible, therefore, to identify them as true skin. In one section there was observed what appeared to be a rudimentary hair follicle which contained no hair. By the use of silver stains, we discovered no evidence of neuro-epithelium.

There were some points of special interest in the microscopic examination: Several cysts were present which contained stratified, columnar and transitional epithelium (fig. 3). In some instances the cysts were empty. In others they contained what appeared to be desquamated epithelium. Still others had an eosin-stained secretion.

There were two hemorrhagic areas, one of which showed a more advanced degree of organization than the other. In the older of these great numbers of macrophages were observed to be carrying blood pigment. In the other the hemorrhage issued into a previously angiomatous region. There was some necrosis of the tissue adjacent to the hemorrhagic areas, and in these places were seen many old polymorphonuclear leukocytes, with a surrounding wall of lymphocytic infiltration.

There was no evidence of malignancy in any of the sections studied.

PATHOLOGIC STRUCTURE

The tumor under discussion contained elements representative of all the primary embryonal layers, but since it contained no formed organs it was necessary to classify it as a teratoid tumor. Both Lexer and Portugal stated that true teratomas are less common than teratoids. Kuznetsoff maintained that in the retroperitoneal area the opposite is true. An analysis of the cases presented here supports this view: Nearly two thirds of the growths were true teratomas. G. W. Nicholson has shown that several studies seem to report inaccurately the presence of formed organs. An epithelium-lined cyst containing an occasional goblet cell does not justify concluding that the tumor contains large intestine.

Structurally the tumor under study was not unusual. The great number and approximate equality in size of the cysts were noteworthy. Cysts containing three kinds of epithelium have been recorded by Lexer, Pilliet, Dickinson and others. The majority of tumors contain bone, but a roentgenogram of the tumor described here failed to reveal its presence. The area of cartilage was unusually small. No cholesterol crystals were detected by fresh smears.

The fact that one area of hemorrhage appeared to be further organized than the other gives rise to the thought that there may have been recurrent hemorrhages.

The size of the tumor under discussion was about the same as that of the growth in the case of Gross, which was the smallest previously recorded. That tumor also was located in the right upper quadrant, and the patient recovered after operation. Lexer stated that the majority

of the tumors were located in the left upper quadrant, and, indeed, we were able to find only five previously reported that were located in the right upper quadrant.

CLINICAL SURVEY

A review of the cases studied shows some points of clinical interest. While there is no information available, it is probable that in few of the cases was a diagnosis made before operation or autopsy.

A tumor of this type is found usually before the patient reaches the age of 30. There were but three cases reported in persons past that age. Forty per cent of the patients were in the first decade, and 34 per cent, in the third. Distribution was nearly even between the sexes, fifteen being males and eighteen females.

An abdominal mass was the chief complaint in most instances. Pain was the next most frequent symptom, ranging in severity from a vague backache to the acute pain seen in the case here described and probably related to the hemorrhage found in the tumor bed. Vomiting and constipation were noted occasionally. These were due, in all probability, to external pressure. Fever was mentioned only once.

Rapid growth of the tumor was reported by Tillaux and was taken to indicate malignant change. Gradual loss of weight was the rule, and cachexia was seen in the terminal stages.

Physical examination invariably showed a tumor. The size ranged from that of a lemon to that of an adult head; the growth was usually located in the left upper quadrant, and generally was fixed. Edema of the extremities was recorded in several cases, and with a small tumor this might easily give a clue to the location of the lesion.

There are a few studies that might be of diagnostic value: A flat roentgenogram of the abdomen might reveal pieces of bone in the tumor. A roentgenogram taken after a barium enema would give valuable information as to the relative position of the tumor. One taken after the retroperitoneal injection of air, after the method suggested by Cahill, might aid further in localization. Urograms and pyelograms would help to rule out renal lesions, although they might show evidence of distortion due to external pressure. It is noteworthy that although such a tumor is in close juxtaposition to the kidneys, renal symptoms (except in the case reported by Roux) have been absent.

The chief differential diagnosis must be made from hypernephroma and retroperitoneal sarcoma. The more rapid evolution of the mass, the early onset of cachexia and the early metastasis point to the more malignant lesions. Often a hypernephroma gives rise to early renal symptoms and causes defects in the roentgenogram of the urinary tract. The presence of a febrile reaction is common in cases of sarcoma.

There are but two methods of treating these lesions. The first is surgical exploration and the removal of the tumor, either in whole or in part. In the cases here reviewed, twenty-three of the patients were operated on, of whom only seven survived—an operative mortality of 70 per cent. Of the seven who recovered, one died eight months later. Only a biopsy specimen had been removed from this patient at operation. In the remaining six patients the tumor was entirely extirpated, and as far as can be stated from the information available, there were no recurrences or further symptoms. Most of the deaths followed attempts at removal of a very large lesion. The cause of death in the majority of cases was hemorrhage and shock. Some of the patients might have been saved had modern methods of intravenous infusion and transfusion been available.

The other possible method of treating such a tumor is by interstitial irradiation. There is little information available on the subject, although it is well known that the tumor is highly radioresistant. The method might have definite application, however, in those instances in which the tumor appears to have undergone malignant degeneration. In a tumor which has been incompletely removed or from which a biopsy specimen has been taken, there is danger of seeding. From the malignant behavior of such seedings it must be deduced that they have taken in their growth a more anaplastic character than the cells from which they arose, in which case they should be more radiosensitive. We believe that all incompletely removed tumors and those from which biopsy specimens have been taken should have adequate roentgen therapy.

SUMMARY

The literature on retroperitoneal teratoma is reviewed.

A new case of retroperitoneal teratoid tumor is presented. The tumor was extirpated, and the patient was well six months after operation.

The diagnosis and treatment of lesions are discussed.

Dr. I. S. Ravdin granted us permission to discuss his case in this paper; Drs. A. E. Bothe and Charles C. Norris reviewed the slides, and Mr. Kitamura, a student at the university, supplied the translations of Japanese articles.

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TREATMENT OF COMPOUND FRACTURES

RESULTS IN ONE HUNDRED CASES OF COMPOUND FRACTURES OF THE TIBIA

ELBERT H. CALDWELL, M.D.

NEW YORK

The result of any surgical procedure depends almost as much on the surgeon and his application of it as it does on the merits of the procedure itself. In no field is this more true than in the treatment of compound fractures. Here each fracture presents an individual problem, no two being exactly alike in any of the many particulars which affect the method and result of treatment. Even if one cannot or should not adopt a standard routine procedure for all fractures, it does seem that the treatment of so common and serious an injury should be more standardized than it is today. There is varied and conflicting counsel in textbooks and journals, and even in the large surgical services there is usually no standardized method of treatment. The results obtained by any of the various methods are not satisfactory. Cotton said: "Judging from what I see of end results, I fear that the problem of handling compound injuries needs constant attention and constant emphasis." In this situation it behooves every one periodically to review and critically and honestly evaluate the end-results of whatever method or methods he is using. I have tried to do this for the fractures treated in the first surgical division at the Bellevue Hospital during the past ten years. Because they are the most numerous and offer the most favorable opportunity for comparing different methods, this review has been limited to compound fractures of the tibia. During the past ten years 100 such fractures have been treated on which the records are complete as far as immediate results are concerned. Final results as determined by a follow-up study of more than one year were obtainable in 72 cases. These fractures were treated in a general surgical service by various methods by numerous surgeons and house officers. While this has many disadvantages, it does offer an opportunity to compare different methods.

The results have been bad. There have been numerous infections, several amputations and a few deaths. Part of this may be blamed fairly on the type of patient coming to a large city hospital. Many are addicted to the use of alcohol, many have eczema or ulceration of the legs and nearly all have dirty skin and clothing. However, most of the blame for the bad results must rest squarely on the surgeon. That these

results are not peculiar to this service is evident from a study of the literature and by results seen elsewhere. Hey Groves said: "The results of treatment are extremely bad."

The chief problem in treating these injuries is the prevention of serious infection. There are many factors involved which do not lend themselves to statistical study. However, by analyzing a large number of cases of this type of fracture, one should be able to evaluate to some extent the importance of certain factors. In 23 of the cases at the Bellevue Hospital some degree of infection developed, varying from a mild subcutaneous cellulitis, or a persistent sinus, to violent sepsis.

The most important factor of all, as far as infection is concerned, is promptness of treatment. This is only partly under the control of the surgeon, but its importance should be strongly and repeatedly emphasized, so that there will be no unnecessary delay, such as results from transferring the patient from one hospital to another, etc. Of the patients entering the Bellevue Hospital more than two hours after the accident, infection developed in 50 per cent, whereas of those brought in less than two hours after the fracture occurred, infection developed in only 20 per cent. Admission to the hospital from one to two hours after the accident does not mean prompt treatment. Ideally the patient should be on the operating table within an hour after the accident. This factor is so important that I believe it is a mistake to lay too much stress on the treatment of shock and of the patient's general condition, as is done in most textbooks and medical schools. Débridement, reduction and immobilization of a fracture need not be shocking procedures and can well be carried out coincidentally with the treatment of shock. In fact, I think that it is a part of this treatment. Certainly a patient will recover from shock more readily with the fracture reduced and securely immobilized than he will in uncomfortable, inefficient temporary splints. The time element is so important that débridement should be carried out without delay while the patient is receiving infusion or transfusion and other measures to combat shock.

Every one agrees that débridement and mechanical cleansing of the large wounds communicating with a fracture should be done when the patient is received reasonably early. However, there is a difference of opinion as to whether anything is gained by débridement of the small puncture wounds made from within outward by spicules of bone or by the sharp edges of larger fragments. These wounds are small and innocent looking, the fragments have slipped back into more or less good position, and it is a temptation to apply a little iodine, cover the wound and treat the injury as a simple fracture. Estes advocates this simple course, and as evidence that others besides my co-workers and me do not always practice what they preach, Leland reported débridement of only 12 of 22 wounds. However, the size of the wound bears little relation to the damage to the parts beneath, and bits of dirt or

clothing may have been pulled into even a small opening. Therefore, we believe there should be no compromise. Débridement and mechanical cleansing should be done of all wounds communicating with a fracture, no matter how small. Cotton, Foster, Speed and Wilson agree with this. We had 27 cases of fracture which were seen early in which the wound was less than $\frac{1}{2}$ inch (1.3 cm.) in length. Débridement was done in 7, and infection developed in only 1; débridement was not done in 20 cases, and infection developed in 5. Thus the incidence of infection was cut almost in half by débridement. It is reasonable to suppose that the smaller and cleaner wounds were the ones not subjected to débridement, making the decrease in the rate of infection even more striking.

Many writers speak of the danger of further contamination of the wound while scrubbing, owing to soap and dirt being carried into the wound. Some advise covering the wound and not attempting to scrub the edges. Leaving the most important part of the operative field untouched seems entirely illogical to us, and we believe that the danger can be obviated by scrubbing the wound under a constant stream of water. The direction of flow is always away from the wound, and there is but little chance of carrying dirt into it. The process should be just as thorough and conscientious as the cleaning of the surgeon's hands. Asepsis is only as strong as the weakest link in the chain, and it is most unreasonable to spend eight or ten minutes by the clock scrubbing and disinfecting the hands, covering them with rubber gloves and then operating in a field that has been carelessly cleaned and painted with some confidence-inspiring antiseptic. The operative field should be scrubbed for at least ten minutes under a constant stream of water, cleaned with alcohol and ether and then painted thoroughly with iodine or some other antiseptic. The edges of the skin and all devitalized tissue should be excised and the wound again irrigated.

After cleansing and débridement, the question arises whether to close the wound, drain it, pack it open or start immediate treatment with a diluted solution of sodium hypochlorite. Cotton, Estes and Stimson advise loose suture of the cleaner wounds, without drainage. Wilson and Cochrane advise suture only in the cases in which treatment is given within twelve hours after injury and in which the surgeon feels absolutely certain that mechanical sterilization has been obtained. Gurd uses the bismuth-iodoform paste treatment popularized during the World War. This is essentially the same as the Orr treatment, as the mild antiseptic value of the bismuth-iodoform paste is of no importance. Foster leaves the wound open and treats immediately with a diluted solution of sodium hypochlorite. Of the cases of fracture at the Bellevue Hospital in which the patient was treated soon after injury, débridement and suture without drainage were done in 34; of these, infection developed in 7. 21 per cent. Twenty-five wounds were left open without drains or packing; of these, 5, or 20 per cent, became infected. Of the

12 packed open, infection developed in 2, or 17 per cent. Thus it is seen that statistically there is little difference between suturing, packing and leaving the wound open. Except for the fractures seen soon after the accident, packing is the safest treatment. Little is lost by packing as the wound heals by granulation before bony union occurs. One important fact is brought out by the 7 cases in which suture and drainage were done; the wound in 3, or 43 per cent, became infected—more than double the incidence by any other method. The rubber tissue drain inserted "because there is oozing" or "to allow the escape of serum" is not only useless but definitely harmful. It acts as a foreign body, increasing the exudation and preventing the tissues from exerting their strong defensive mechanism. All these wounds are contaminated, but if the tissues are given a chance they will overcome what organisms remain after débridement. This is becoming universally recognized as regards the peritoneum, joints and blood stream, and we believe that it holds true of bone and muscle. There should be no compromise, no middle ground. Either the wound should be closed, or it should be left open and packed lightly with gauze treated with petrolatum.

All of our patients were treated either by traction or with plaster splints or casing. Statistically, there is little difference in the incidence of infection, 30 per cent of those treated by traction and 24 per cent of those treated in plaster becoming infected. We believe that when the fragments can be held in good position in plaster, the secure immobilization is a great advantage in decreasing the incidence of infection and delayed union. Three of the 21 patients treated by traction had delayed union, whereas only 1 of the 63 treated in plaster failed to get bony union within six months.

Numerous surgeons have had the temerity to apply internal fixation to these open, potentially infected wounds. According to Wilson and Cochrane, the method has been superseded and should be used only in rare and exceptional cases. Hey Groves is more vehement. He stated: "I say quite deliberately that I regard the plating of an open fracture as a surgical crime." In the face of this, Foster reported results in a large series of fractures from Sherman's clinic which no one else has approached. Of 304 fractures, he plated 146 and not only had no severe infections but had fewer persistent sinuses in the cases in which plating was used than in those in which it was not employed. Recently we plated a few compound fractures with good results, but we believe that the method should be reserved for the exceptional fracture, i. e., the fracture seen soon after injury in which mechanical cleaning is satisfactory and in which reduction cannot be retained by other methods.

We were forced to amputate in 5 cases. In 2 of these primary amputation was done because of nonviability of the foot. One man refused operation on admission to the hospital, and infection developed, necessitating amputation. In a boy of 12 years with extensive avulsion

of the skin and soft parts by a crushing injury, a severe infection developed, and the leg was amputated on the fourth day. Another fracture involving the ankle joint was manipulated in the presence of active infection, which is extremely poor surgical judgment, and a violent flare-up of the infection occurred, necessitating amputation.

In this series of 100 cases there were 8 deaths. Five were due to associated injuries and 1 to pneumonia three weeks after the fracture, so that only 2 deaths may be directly attributed to the injury. In 1 of the fatal cases the wound was closed loosely without drainage, and the fracture was immobilized in plaster splints. In the other débridement and loose suturing were done after the insertion of two soft rubber drains. A posterior molded splint was applied. The wound was infected, and amputation on the seventh day did not save the patient's life. The two surgical errors in this case—partly closing and draining the wound and poor immobilization—undoubtedly contributed to the fatal outcome. A posterior molded plaster splint is an absolutely useless gesture toward immobilization, yet for some queer psychologic reason it is one of the most frequent methods of splinting. The splint always breaks at the knee and ankle because a flat strip of plaster has practically no resistance to bending in the direction of its flat surface; also it is applied over the irregular thick soft parts of the calf rather than over the medial surface where the bone is superficial. In minor fractures, where one strip of plaster is to be relied on it should be applied on the lateral or medial surface, and the lower end passed under the instep and over the dorsum of the foot. Applied in this way it at least has some effect.

CONCLUSIONS

I have nothing new or startling to report in the treatment of these fractures, but a fairly large series of fractures is reported in order to emphasize the seriousness of this injury and the great room for improvement in results obtained here and elsewhere. The mortality, loss of function, period of hospitalization and economic loss are greater than for surgical diseases which receive much more attention and thought.

After reviewing the subject I feel more strongly than ever that this type of fracture presents an urgent surgical emergency. Débridement and thorough cleansing of all wounds that communicate with a fracture should be done no matter how small or clean they seem. The apparently clean wounds that are seen soon after injury in which mechanical cleansing is adequate should be sutured without drainage. Where treatment has been delayed or is not adequate for any reason, the wound should be left wide open and packed lightly with gauze treated with petrolatum. Immobilization in a plaster is superior to traction suspension in that it lowers both the incidence of infection and the incidence of delayed union or nonunion.

A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.
LOS ANGELES

FRANK HINMAN, M.D.
SAN FRANCISCO

ALEXANDER VON LICHTENBERG, M.D.
BUDAPEST, HUNGARY

ALEXANDER B. HEPLER, M.D.
SEATTLE

ROBERT GUTIERREZ, M.D.
NEW YORK

GERSHOM J. THOMPSON, M.D.
AND

JAMES T. PRIESTLEY, M.D.
ROCHESTER, MINN.
AND

VINCENT J. O'CONOR, M.D.
CHICAGO

(Concluded from page 210).

BLADDER

Physiology.—Rubritius⁵² stated that the hollow muscular organs behave according to the laws which govern all the nonstriated muscles. The peristalsis of the hollow tubiform organs as well as the phases of filling and evacuating of hollow spherical organs can be explained by these principles.

During the phase of retention the wall of the bladder expands by the accumulation of urine, while its resistance remains the same. During this phase the internal pressure of the abdominal cavity is transmitted only partially to the internal pressure of the bladder on account of the tonus, that is, the resistance of the wall of the bladder. The capacity of the bladder is dependent on the tonus of the moment. When the maximal capacity has been reached, the contractive stimulus passes into the most extended muscular zone, that is, into the detrusor muscle.

With the contraction of the detrusor muscle, the sphincter relaxes. The tonus of the sphincter and the tonus of the detrusor muscle are

⁵². Rubritius, Hans: Die Physiologie der ableitenden Harnwege, Kong. d. internat. Gesellsch. f. Urol. 6:499-574 (Sept.) 1936.

dependent on each other; therefore, the sphincter remains open until the detrusor muscle has contracted completely, while the closing contraction of the sphincter puts an end to the contraction of the detrusor muscle. If the tonus of the sphincter is abnormally high, the closing contraction begins prematurely, and residual urine remains in the bladder. The presence of residual urine has a compensatory effect, because a bladder holding residual urine can work more economically and stand a higher pressure, so that it may keep up its function in spite of the obstacle to the outflow of urine.

While the bladder is contracting (transporting phase of the bladder), the peristalsis of the upper portion of the urinary tract ceases. The pelvis of the kidney and the ureter remain in a state of tonic extension (phase of retention). In the meantime the orifices of the ureters do not open, and urine flows out of the collecting tubes into the calices and into the pelvis of the kidney. The alternation of the phases of the bladder with those of the upper part of the urinary tract is regulated by reflexes. Any disturbance causes a vesico-ureteral reflux or upward flow.

Recent research has demonstrated that the resorptive efficiency of the mucous membrane of the urinary passages increases with the increasing dilatation of the mucous membrane. Gruber has confirmed the statements of former research workers that a close relation exists between the capillaries and the epithelium of the mucous membranes. This is especially true within the fornix calicis. It is known that the fornix calicis is the most extensible part of the urinary tract. Macroscopic rupture of the mucous membrane of the fornix calicis is of great importance in urinary retention, but there is no reason to look on this rupture as a physiologic phenomenon. If the mucous membrane in the fornix stretches to such an extent that there is utmost thinning of the epithelial cells although rupture has not yet occurred, this mucous membrane becomes permeable.

Urinary passages are, from a physiologic point of view, a closed system, the single morphologic units of which are working hand in hand. The connection of this system with its headquarters, the parenchyma of the kidney, seems to be very ingenious and enables undisturbed cooperation between them. In the urinary passages muscular action is completed by resorptive action. While the physiologic analysis of the former can be considered ideal, new questions are arising with regard to resorptive functions. Their importance from the standpoint of metabolism, the entire body and the connection with the minute collecting system of the kidney with the secretion of this organ are no doubt of great importance for future research.

Calculus.—Hueck⁵³ in ten years performed 171 operations for stone in the bladder. A previous operation had been performed to remove calculi in 14 of these cases, and in 1 case 2 previous operations had been performed. A single stone is usually found, as was the case at 50 operations on 44 patients. The average interval between surgical intervention and reformation of the stone was four years and eight months; in 1 instance it was less than a year. Because of the frequent adhesions between the peritoneum and the bladder, the author advised operation by the perineal route for recurrent calculus with the patient under sacral anesthesia. Thirteen of the patients were men, and 1 was a woman who had a vesicovaginal fistula. In 3 other cases of stone in women, vaginal fistulas were also present. This led the author to think of catarrh of the bladder as a predisposing factor of formation of calculi.

Of the 171 operations, only 10 were performed on females, whose ages ranged from 7 to 75 years. In Professor Olpp's series of cases of vesical calculi from the same hospital, 4 of the patients were women and 201 were men. Twenty of the author's patients were boys. In a series of 100 recent cases, 9 patients died within one month after the operation. This figure included elderly persons and those in whom complications developed. He had another series of 45 operations without a death.

In the author's opinion there has been no decrease in the number of cases of vesical calculus in recent years. Regarding the cause, he thought that hypothetically the body constitution, the composition of water and vitamin deficiency may play a rôle; ankylostomiasis, malaria and the dysenteries are listed among the predisposing causes. In this connection, Hueck commented on the rarity of cases of stones in Europe at present compared with their frequency in the Middle Ages.

Digby⁵⁴ stated that litholapaxy takes much time and patience. The actual procedure for stones over 1 inch (2.5 cm.) in diameter may consume from three quarters of an hour to a couple of hours. This compares unfavorably with the twenty minutes or less required for suprapubic cystostomy, but the extra time involved is well repaid by the benefits to the patient. Open warmed ether administered by a pump is the routine anesthetic. The table is slightly tilted so that the head is lower, and there has not been any difficulty with bronchitis in this class of case. From a theoretical point of view, sacral anesthesia should be ideal, as it should produce anesthesia of the bladder and urethra and

53. Hueck, O.: Beitrag zur Blasensteinerkrankung. *Chinese M. J.* 50:833-836 (June) 1936.

54. Digby, K. H.: Observations on Litholapaxy. *Chinese M. J.* 50:837-845 (June) 1936.

relaxation of the detrusor fibers. It has been tried in a few cases and has worked out badly. Contrary to physiologic theory, the bladder seems to contract around the stone and interfere with manipulations. Spinal anesthesia is mentioned only to be condemned, at any rate, for the neglected patient with a large stone of long standing and possibly damaged kidneys. Such cases form the bulk of the cases of vesical calculus. Spinal anesthesia lowers the blood pressure, and anuria may follow. Digby stated that he had encountered this condition more than once when he had been called to see a patient in consultation after operation by others. Spinal anesthesia has not been employed for removal of a vesical calculus in his clinic.

Litholapaxy is contraindicated in the following circumstances: 1. When there are signs of renal failure, such as suppression or extreme diminution in excretion of urine or a glazed and dry tongue, or the value for blood urea is more than 50 mg. per hundred cubic centimeters. 2. When the prostate gland is felt to be much enlarged on rectal examination or has been producing symptoms. In this case a suprapubic cystostomy with extraction of calculi should be followed in a week by suprapubic enucleation of the prostate. In these cases there are usually multiple calculi. More than one stone in an old man should always raise the suspicion of enlargement of the prostate gland, as should also the discovery of residual urine. 3. When there is a stricture of the urethra of any marked degree. Although the stricture can be dilated and the litholapaxy proceeded with, the more prudent method is to accompany the dilation with suprapubic cystostomy, unless the stricture is slight. 4. When the stone has caused a penetrating ulcer of the wall of the bladder so that extraperitoneal extravasation of urine has occurred, or a vesicosuprapubic fistula or a vesicorectal fistula has formed. 5. When advanced cystitis is present to such a degree that the urine is foul smelling, brown and ammoniacal and the bladder cannot be distended with fluid. In such cases suprapubic cystostomy is wiser. 6. When the stone is large. This is usually but not always a contraindication for litholapaxy. Very large stones have been crushed by experienced surgeons.

A surgeon should always be prepared to deal with any possible accidents. The posterior part of the urethra or the neck of the bladder may be perforated in passing one of the instruments. The wall of the bladder may be nipped and crushed. Severe crushing of the wall can be avoided by rotating the blades in the initial position before crushing the stone. The blade of the lithotrite used for the male may break or, worse, may bend. In the first case the lithotrite can be withdrawn without the blade. The broken blade has to be removed suprapubically. In the second case, after the bladder has been opened suprapubically, the blades should be protruded as far as possible and

an attempt made to detach the bent blade with a hack saw. If the blades cannot be protruded far enough, the staff must be sawed through with a hack saw and the bent distal part of the lithotrite extracted through the suprapubic wound. The blades may jam on a cystine calculus. A fragment of stone may be overlooked at litholapaxy and become impacted in the urethra before the subsequent cystoscopy.

Kya⁵⁵ reported the results of a chemical analysis of vesical calculi in 42 cases. In 16 cases (38.4 per cent of cases analyzed) the stones contained uric acid as the chief constituent; in 18 cases (43.2 per cent of cases analyzed) there were mixed stones containing uric acid, calcium oxalate and calcium phosphate in balanced proportions. He stated that mixed stones are the commonest variety, and next to them are the uric acid stones. Rarely are pure stones of one constituent only found. The result of analysis of this series agrees with the figures of Jones in England, of Newcomb in India and of Thomson in Canton in that stones containing uric acid and urates as the chief constituent form a higher percentage than other stones.

Oxalate stones are seen in children, while uric acid or urate stones are obtained from middle aged or elderly patients.

The visibility of vesical stones of different chemical composition in roentgenograms has been dealt with. Kya had only 1 pure uric acid stone which was translucent to the roentgen rays. All other uric acid stones showed well in the roentgenograms, because they contained a certain proportion of calcium. Pure cystine is invisible in body tissue to detection by roentgenographic examination, but the stone which was 96 per cent cystine, 0.8 per cent calcium and 0.6 per cent phosphate showed distinctly in the roentgenogram. The opacity was probably due to the contained calcium.

Lett⁵⁶ stated that during the thirty year period previous to 1934 there were 2,781 patients with stone in the urinary tract admitted to the London Hospital. A study of this series suggests that stone in the urinary tract as a whole is twice as common in the male as in the female. The sex of the patients with stone in the kidney was fairly evenly distributed, as 849 of the patients were males and 719 were females. Of those with stone in the ureter, 353 were males and 179 were females, so that the former outnumbered the latter in the proportion of 2:1. However, when the patients with stone in the bladder were considered, there was a very great preponderance of males, as only 8.2 per cent of the patients were females.

55. Kya, L. T.: The Composition of Vesical Calculi, *Chinese M. J.* **50**:797-806 (June) 1936.

56. Lett, Hugh: On Urinary Calculus, with Special Reference to Stone in the Bladder, *Brit. J. Urol.* **8**:205-232 (Sept.) 1936.

During the last ten years of the period under review there was a considerable increase in the number of patients with urinary stone admitted to the London Hospital, for, including those with stones impacted in the urethra, they numbered 1,085 as against a total of 778 admitted from 1915 to 1924, an increase of nearly 50 per cent. The number with renal calculi rose from 485 to 644; with ureteral calculi, from 130 to 208, and with vesical calculi, from 140 to 212. However, the number of patients with urethral calculi decreased from 23 to 21. Instead of an increase in the number of children with stone, the incidence fell from 69 during the period from 1905 to 1914, to 27 during the last ten years, largely owing to a diminution in the number of patients with stone in the bladder and urethra. It is interesting to find a definite increase during the five years that followed the World War, particularly in the number of patients with stone in the kidney.

Stones were found in the kidney in 1,568 patients, in the ureter in 532 and in the bladder in 608. The total of 2,781 patients in the series is completed by 73 with stone in the urethra. Thus there was a combined total of 2,100 persons with stone in the kidney and ureter as compared with 608 with stone in the bladder.

The urine of 750 consecutive patients with stone in the urinary tract was examined. This group was made up of 487 with stone in the kidney, 140 with stone in the ureter and 123 with stone in the bladder. The reaction of the urine was acid in 72 per cent of all instances in which it was examined. No report was made on the reaction of the urine of 4 of the patients with renal calculus, but that of 347 was acid, that of 41 was neutral and that of 95 was alkaline. Repeated examinations of the urine of a number of patients were made; the reaction of specimens of 103 varied on different occasions, while the first specimen of 67 was acid. Reports were made on the urine of 139 patients with calculus in the ureter; that of 102 gave an acid reaction, that of 10 was neutral and that of 27 was alkaline. Repeated examination of the urine of 29 patients disclosed varying reactions, while the first specimen of 24 was acid. The urine of 88 of the 123 patients with vesical calculus was acid, that of 10 was neutral and that of 25 was alkaline. There were 25 patients whose urine gave different reactions on repeated examinations, and 22 whose first specimen was acid.

Tumor.—Gehrmann⁵⁷ stated that prolonged exposure to relatively low concentrations of certain intermediates produced during the manufacture of dyes and classified as aromatic amines is known to have caused the development of tumors of the bladder in certain persons. The carcinogenic compounds already mentioned enter the circulation

57. Gehrmann, G. H.: Papilloma and Carcinoma of the Bladder in Dye Workers, *J. A. M. A.* **107**:1436-1438 (Oct. 31) 1936.

through three routes: (1) respiratory, (2) cutaneous and (3) gastro-intestinal. It is generally agreed that the most important route of entrance is through the respiratory tract, in the form of dust and fumes. Absorption through the gastro-intestinal tract is probably of the least importance. However, it must be remembered that present knowledge indicates a long period of exposure to low concentrations as an etiologic factor. Therefore, any absorption through the gastro-intestinal tract should be considered as of more or less importance, despite the low solubility of these compounds.

The classic symptoms of tumor of the urinary bladder are hematuria, frequency, urgency, burning and pain. These symptoms as a group occur in Gehrmann's experience only in those cases in which the condition is well advanced. It has also been his experience that cystoscopic examination is the only safe method of early diagnosis. The growths may be single or multiple, papillary or sessile, infiltrating or noninfiltrating, ulcerating or nonulcerating, malignant or benign. In Gehrmann's group of 63 cases of tumor of the urinary bladder, 38 were carcinomas.

The histologic structure of the aniline tumor does not differ from that of tumors of unknown etiology. The aniline tumor occurs in all gradations, from the slowly growing villous papilloma, which may remain latent for many years, to the rapidly growing destructive and anaplastic carcinoma, which produces early and widespread metastasis.

Preventive measures are divided into two groups: plant operative control and medical control. The plant operative measures consist of manufacturing processes that provide complete protection against any exposure to dust or fumes. Every applicant for work in regions in which he will be exposed to aniline, alpha and beta naphthylamine and benzidine should have a cystoscopic examination in addition to a regular complete physical examination. Any disease of the genito-urinary system is a contraindication to employment, as is a family history of cancer and a history of hematuria or venereal disease. No applicant for this type of work should be accepted who is less than 21 or more than 40 years of age. All workers should have a complete physical examination and cystoscopic examination once a year. Every three months there should be a complete urinalysis and, on the appearance of macroscopic or microscopic blood, cystoscopic examination is indicated.

The prognosis is good in cases of benign tumor. However, further growths may occur at any time and may be primarily benign or malignant. The prognosis in cases of malignant aniline tumor of the bladder in general is not favorable. Simon expressed the belief that this type of growth is biologically different, runs a slower course and responds better to therapeutic procedures.

Dart⁵⁸ reported a study of the cell types and the methods of grading of the cases in the Carcinoma Registry of the American Urological Association. Since the opening of the registry in May 1927, more than 1,400 cases have been reviewed. Follow-up reports have been obtained each year on all but 77 cases. One thousand, two hundred and twenty-four of the 1,400 cases were used as the basis of this report.

With few modifications, the present criteria for grading tumors of the bladder used in the registry office are the same as those adopted by the original registry committee in 1927. These criteria are based on a combination of clinical factors and the histopathologic appearance of the specimen. For the purpose of these studies this has been designated as the registry grade. As a check on the efficiency of the registry grade, the registrar chose other criteria based solely on the histopathologic appearance of the tumor. This is referred to as the histologic grade. The underlying principles used in establishing the histologic grade are much the same as those which have been followed more or less consistently by all workers since Broders first announced his method.

The final grade and status of the 1,224 epithelial tumors of the urinary bladder were as follows: The registry grading (clinical data and cellular character) revealed 46 papillomas and 65 carcinomas of grade 1, 347 carcinomas of grade 2, 584 carcinomas of grade 3 and 182 carcinomas of grade 4, making a total of 1,224. The histologic grading (cellular character) revealed 101 papillomas and 200 carcinomas of grade 1, 266 carcinomas of grade 2, 459 carcinomas of grade 3 and 198 carcinomas of grade 4, making a total of 1,224.

Based on all of the facts found, it is believed that the present registry grade may be simplified, to advantage, as follows:

Grade 1. Papillary carcinoma. This type includes all papillary tumors in which there is no clinical evidence of infiltration and in which no obvious infiltration of the pedicle or the wall of the bladder can be demonstrated on histopathologic examination, and most of the cells are typical in appearance and arrangement.

Grade 2. (a) Papillary and infiltrating carcinoma. Obviously this type includes infiltrating papillary tumors and carcinomas in which the papillary structure is recognizable but most of the cells are atypical in appearance and arrangement. (b) Infiltrating carcinoma. This type includes the nonpapillary squamous cell carcinomas in which the cells are fairly uniform in size and type or have a tendency to form keratohyalin and epithelial pearls.

58. Dart, R. O.: Grading of Epithelial Tumors of the Urinary Bladder: A Study of the Cell Types and the Methods of Grading of the Cases in the Carcinoma Registry of the American Urological Association, *J. Urol.* **36**:651-668 (Dec.) 1936.

Grade 3. Nonpapillary infiltrating carcinoma. This classification refers to the very anaplastic infiltrating carcinomas. Practically all of the cells are atypical in appearance, and there is very slight or no differentiation.

Although definite conclusions cannot be made concerning the efficiency of grading of vesical tumors until more growths have been checked for a longer period, these studies indicate that it is impracticable to attempt the segregation of tumors of the bladder into definite groups corresponding to their cell types. For all practical purposes, epithelial tumors of the bladder may be classified as papillary, papillary and infiltrating, and infiltrating. Carcinoma of the bladder cannot be graded on the basis of cell differentiation alone. The mortality for the more differentiated types, such as acanthoma, is practically the same as that for the less differentiated squamous cell tumors. The most practical method of grading is based on a combination of physical and histopathologic observations.

Colston and Leadbetter⁵⁹ studied 98 cases of extensively infiltrating tumor of the bladder in which necropsy was performed at the Johns Hopkins Hospital; they attempted to correlate the history, methods of treatment and postmortem observations. The growths were exclusively epithelial tumors, with the exception of 1 sarcoma. Metastasis occurred in 56.1 per cent, and in 10 cases the tumor extended through the wall of the bladder without producing metastasis. Tables are given on each grouping and on the duration of symptoms compared with metastasis and extension, organs involved by metastasis, the pathway of metastasis, the comparison of treatment with occurrence of metastasis and the cause of death in operative cases. The importance of ureteral obstruction with resulting infection and destruction of renal tissue either from direct invasion of the tumor or from sclerosis of the ureteral wall due to scar tissue has been emphasized. A particular study of the microscopic structure of the tumors was undertaken to determine if they could be classed according to the cellular structure and architecture of the tumor as a whole. A tentative classification has been made, consisting in order of frequency of occurrence of (1) papillary carcinoma, (2) transitional cell carcinoma, (3) squamous carcinoma and (4) undifferentiated carcinoma. All of the tumors studied, with the exception of a few in the papillary group, were graded 3 or 4 according to Broders' classification. The papillary carcinomas revealed the smallest incidence of metastasis and the undifferentiated carcinomas the greatest, with the incidence in the squamous and epithelial groups lying between. The undifferentiated group is charac-

59. Colston, J. A. C., and Leadbetter, W. F.: Infiltrating Carcinoma of the Bladder, *J. Urol.* **36**:669-689 (Dec.) 1936.

terized by extensive and rapid metastasis. The squamous epithelial tumors had a tendency to extend first to the regional lymph nodes, perhaps later involving the liver, lungs or bones, while the other two types of tumors in many instances showed distant metastasis without involvement of the lymph nodes.

As in all series of cases, various types of treatment had been used. It was impossible to state definitely the effects of treatment in the various groups, but the author's impression was that the undifferentiated type and the papillary type responded best to radium and high voltage roentgen therapy, as evidenced by the degree of destruction of the original tumor. The local response of these exceedingly malignant tumors to radium and high voltage roentgen therapy, particularly when more modern methods of treatment are applied, is extremely encouraging, and it is hoped that still better results may be obtained. Radical surgical procedures, including total cystectomy, should be reserved for those growths which have proved resistant to a thorough course of high voltage roentgen therapy and radium therapy.

Barringer⁶⁰ stated that the best statistics on carcinoma of the bladder indicate only between 25 and 30 per cent five year cures. This leaves a residue of 70 or 75 per cent of cases in which the patient succumbs to the disease. This means that one should not be satisfied with the present day methods of cure, and this is the reason new operative and irradiation devices are constantly cropping up.

When these cases are considered individually, total cystectomy comes first. Barringer stated that if the operation is performed, suprapubic implantation of the ureters is preferable to the implantation into the intestines, because it is less dangerous. There has been a distinct flare-up in extending the use of external irradiation to the treatment of carcinoma of the bladder. Pfahler has reported a few cures, but his pathologic reports are too inadequate to evaluate these. The statistics of operative removal are impressive. They indicate that the operative removal of carcinoma of the bladder has a definite place in the control of this disease. Its scope appears to Barringer to be limited. It does not seem to be applicable to tumors which involve the trigon too much. His impression is that more urologists in America are controlling vesical tumors by radium implantation than by any other method. Radium with all its faults, and they are many, seems to be able to cure many tumors. Barringer's own trend is definitely away from the suprapubic implantation toward cystoscopic implantation. Further progress in the treatment of difficult infiltrating tumors is probably along lines which combine interstitial irradiation with external irradiation.

60. Barringer, B. S., in discussion on Colston and Leadbetter,⁵⁹ pp. 684-685.

Beer⁶¹ stated that for papillary and infiltrating carcinoma partial cystectomy after electrocoagulation of the surface of the tumor, with or without ureteral transplantation into the bladder, or total cystectomy with implantation of the ureters into the skin or the sigmoid colon are undoubtedly the procedures of choice, and any one who is treating patients suffering from tumors of the bladder should be able to carry out these various procedures. Only by experience will the mortality of the operations in the latter group be diminished. The mortality at present is undoubtedly high for these surgical procedures, not only because the patients are old, as a rule, but usually because they have been neglected for a long time before they come to operation, have more or less damage to the upper part of the urinary tract and perhaps are suffering from local or distant metastasis.

In Beer's recent monograph on tumors of the bladder, a review of the later cases, plus those in his original report, confirmed his original conclusion presented at the International Congress at Brussels in 1927, and his results as far as five year cures are concerned are considerably better than those published by the Carcinoma Registry of the American Urological Association.

For instance, of 88 persons with papillary and infiltrating carcinoma of the bladder treated prior to 1930, 15 died. Of the 73 patients discharged from the hospital, 65 could be controlled. If one subtracts the 8 who were lost from observation and the 15 who died as a result of the operation or causes associated with the operation, 65 remain on whose cases one may base the efficacy of a radical surgical procedure, that is, partial resection with or without transplantation of the ureter. In this group of cases in which radical excision was done there were 24 five year cures, or 37 per cent, which is about twice that reported by Ferguson, based on the Washington Registry.

Moreover, in going over a series of cases in which total cystectomy was performed, the tumor having involved the trigon, both ureters and the neck of the bladder, it was found that in the cases in which operation was performed before 1930 there were 57 per cent permanent cures, which is by far the highest percentage, according to Beer, that could be obtained by any method of surgical approach, and is a most encouraging outlook for the future.

Beer stated that the outstanding conclusions one must draw from Dr. Ferguson's report are (1) that vesical tumors are very serious as a group, (2) that as yet there is no uniformity as to the proper method of treatment and (3) that the more radical the therapy the better is the chance of a permanent cure for the patient.

61. Beer, Edwin, in discussion on Colston and Leadbetter,⁵⁹ pp. 687-688.

In view of the fact that implantation of seeds of radon through the cystostomy wound has given five year cures in only 8.8 per cent of cases, whereas partial cystectomy of the bladder has given five year cures in 18.5 per cent, it must be evident that those who rely entirely on the use of radium are not giving the patient with vesical tumor the care he deserves. As has been repeatedly emphasized, every urologist should be able to treat vesical tumors by innumerable methods. For the simpler small tumors and papillomas and occasionally for papillary carcinomas, transurethral treatment with a high frequency current is surely the method of choice, though in the latter group radium seeds introduced transurethrally may be necessary to eradicate the disease.

Bothe⁶² stated that a tumor of the bladder is occasionally well advanced before the patient is studied. In some cases the tumor is in a location that involves considerable risk for surgical removal, or it gives evidence of extensive infiltration. In such cases roentgen therapy should be of great assistance. In the papillary carcinoma the regression established by roentgen therapy facilitates subsequent interstitial irradiation. Irradiation has been used before electrocoagulation for the benign papilloma. It is generally agreed that many benign papillomas have been permanently destroyed by electrocoagulation alone. It is also a fact that follow-up examinations on patients with benign papilloma frequently reveal recurrence. It seems within the realm of possibility that preparatory high voltage roentgen therapy may reduce the incidence of this recurrence.

Higgins reported 5 cases of neoplasm which was primary in and confined to a diverticulum of the bladder in a series of 221 cases of tumor of the bladder which were seen at the Cleveland Clinic. Primary carcinoma of the urinary bladder frequently extends into and involves a diverticulum of the bladder, but a primary neoplasm in a diverticulum is a rather infrequent finding.

In the majority of cases diverticulum of the bladder may be diagnosed readily on cystoscopic and roentgenographic examinations. When blood can be seen spurting from the orifice of the diverticulum, the presence of a neoplasm should be suspected. In 2 cases, after thorough lavage of the diverticulum, persistent filling defects were noted on 2 successive examinations, and preoperative diagnoses were made which were verified at the time of operation. In 1 case the tumor was visualized at cystoscopic examination.

Total resection of the diverticulum containing the tumor is the rational treatment. Whether the intravesical or the extravesical technic is utilized depends on the preference of the surgeon. In this series the

62. Bothe, A. E.: Roentgen Therapy in the Treatment of Bladder Tumors, *J. Urol.* **36**:643-650 (Dec.) 1936.

extravesical technic was used, and the diverticulum was excised completely with a portion of the bladder in the region of the orifice of the diverticulum. In 2 cases in which the ureters were contained in the wall of the diverticulum it was deemed advisable to divide and ligate the ureters and not attempt to reimplant them into the bladder. Although fulguration of the tumor has been employed, radical operation seems preferable.

In the 5 cases reported by Higgins,⁶³ 1 patient with papilloma of the bladder died of a cerebral embolism seventeen months after leaving the hospital, but the papilloma had not recurred up to that time. One patient with carcinoma in a diverticulum died suddenly of pulmonary embolism on the twenty-first postoperative day. One patient with carcinoma in a diverticulum lived one year and six months without recurrence. Another patient died of an unknown cause two years after removal of a diverticulum containing a papilloma. The fifth patient is living without recurrence six months after operation.

Diverticulum.—Babics⁶⁴ stated that 80 of 117 patients with a diverticulum of the bladder observed at von Illyés' clinic had some marked obstruction to the urinary outflow. Thirty-three were operated on. Stones were found in the diverticulum in 8, cancer in 4 and papilloma in 1. Five patients died after operation. The operative procedure has to be adapted to every patient. When the ureter ends in the diverticulum, it should be transplanted. This was done in 6 instances. Sometimes the kidney is so badly infected that it is better to remove it. Von Illyés when necessary performs a prostatectomy and diverticulectomy as a one stage procedure and has never noticed any disadvantage therefrom. One of these patients died from pneumonia after operation.

Cord Bladder.—Gill⁶⁵ gave a brief discussion of neurogenic dysfunction of the bladder with particular reference to cord bladder or that type of dysfunction of the bladder produced by disease of the spinal cord. Two cases of marked vesical paralysis are reported in patients whose only diseases were mild arteriosclerosis and severe diabetes mellitus of long standing. It is believed that the paralysis of the bladder was due either directly or indirectly to diabetes and its effect on the spinal cord, and the reasons for this belief are given. A close cooperation between the urologist, internist and neuropathologist is urged in the study of these extraordinary and unusual cases.

63. Higgins, C. C.: Neoplasms Primary in Diverticula of Urinary Bladder: Report of Five Cases, *Am. J. Surg.* **33**:78-84 (July) 1936.

64. Babics, Antal: Ueber Blasendivertikel, *Ztschr. f. urol. Chir. u. Gynäk.* **42**:395-410, 1936.

65. Gill, R. D.: The Diabetic (Cord)-Bladder, *J. Urol.* **36**:730-739 (Dec.) 1936.

Munro⁶⁶ stated that for purposes of diagnosis, prognosis and treatment cord bladder resulting from all types of injury to the spinal cord should be divided into four distinct groups.

These may be measured cystometrically against the activity of the normal bladder in terms of initial and sustained tonus, the presence and periodicity of emptying contractions, the absolute amount of residual urine expressed in terms of percentage of fill, the storage capacity of the bladder and the reflex and voluntary sphincteric activity.

With these criteria, cord bladders may be classified as atonic, autonomous, hypertonic and normal.

The only permissible end-result of any cord bladder that is due to injury of the spinal cord is either an uninhibited cord bladder in cases of transection of the spinal cord above the sacral segments, an autonomous cord bladder in cases of destructive lesions of the sacral segments or cauda equina or a normal cord bladder in cases of all other types of injury to the spinal cord.

All types of cord bladder are amenable to treatment by tidal drainage, provided the apparatus is adjusted to suit the type of bladder. Except for complications due to misuse of the apparatus, tidal drainage as a method of treatment of cord bladder of any type has no contraindications. Rectal tubes used as indwelling urethral catheters, or mushroom catheters, may be employed indefinitely in conjunction with tidal drainage in either male or female urethras without producing cystitis or urethritis. They must be removed, cleaned and replaced once a week, and care must be taken to avoid the use of those that are too large.

The incidence of decubitus ulcerations is greatly reduced, and the problem of nursing a patient with an injury to the spinal cord is greatly simplified if the patient is kept dry by the proper use of tidal drainage. The incidence of all types of sepsis of the urinary tract in cases of injury of the spinal cord has been reduced from 73 per cent in 33 cases to 15 per cent in 26 cases through the prompt, intelligent and routine use of tidal drainage in the care of the bladder.

Conditions of the Neck of the Bladder.—MacKenzie and Beck,⁶⁷ from a comparison of the 30 specimens of the adult female urethra and the neck of the bladder with 17 similar specimens from children 4 years of age and younger, concluded that chronic inflammation of the urethra and the neck of the bladder is present in a higher percentage

66. Munro, Donald: "The Cord Bladder:" Its Definition, Treatment and Prognosis When Associated with Spinal Cord Injuries, *J. Urol.* **36**:710-729 (Dec.) 1936.

67. MacKenzie, D. W., and Beck, Sidney: A Histopathological Study of the Female Bladder Neck and Urethra, *J. Urol.* **36**:414-437 (Oct.) 1936.

of adults than has heretofore been imagined. Perimucosal structures about the neck of the bladder and the posterior third of the urethra are acquired. These structures simulate prostatic tissue because they take origin from the same type of embryologic tissue and thus have the same inherent properties. The stimulus required for the acquisition of these structures may be: (1) infection within the genito-urinary tract, (2) structural anomalies within the genito-urinary tract and (3) trauma at childbirth. These buds and nests, known as von Brunn's cell nests or buds, so far as they are a proliferation of the mucosal epithelium derive their lumens from the intra-epithelial glands, as seen in the mucosal epithelium in children. Those structures about the neck of the bladder and the posterior third of the urethra, referred to by previous workers as prostatic structures, are considered by MacKenzie and Beck to result from a process similar to cystic disease of the upper part of the genito-urinary tract, better known as pyelitis cystica, ureteritis cystica and cystitis cystica, according to location. They propose to call it cystitis cystica when it occurs about the neck of the bladder and urethritis cystica when it occurs in the urethra.

Pilcher⁶⁸ reported the case of a woman aged 49 who had a malignant lesion in the bladder situated close to the neck. Complete surgical removal of this lesion necessitated resection of most of the trigon of the bladder and division of the urethra about 1.5 cm. distal to the internal sphincter. Resection of the urethra involved the region that is normally occupied by the external sphincter in the male. The distal end of the urethra was then sutured to the remaining portion of the trigon and wall of the bladder, and the neck of the bladder was reconstructed around a catheter. Convalescence was uneventful. After removal of the suprapubic tube, the suprapubic sinus healed promptly. The patient voided satisfactorily and was not incontinent. Urination was comfortable and under perfect control. A surgical procedure of this type at once raised the question of whether or not incontinence would result. Cabot, in discussing Pilcher's report, stated that there is considerable confusion regarding the external urethral sphincter of the female. Some authors describe the external sphincter as the more powerful of the two and as a thoroughly well defined structure. Other authors doubt the existence of such a structure. Recent microscopic studies of longitudinal sections of the urethra made by Shoemaker failed to reveal definitely placed circular fibers such as are regularly to be found in the position of the external sphincter in the male. The fact that incontinence did not result in this case suggests that the control of the urine after complete removal of the internal sphincter may depend on the

68. Pilcher, Frederick, Jr.: Complete Resection of the Vesical Neck in the Female, Proc. Staff Meet., Mayo Clin. **11**:577-579 (Sept. 9) 1936.

widely scattered circular muscle fibers rather than any well defined muscle group properly described as an external sphincter.

Heitz-Boyer⁶⁹ applied the name "inflammatory new growths of the neck of the bladder" to a combination of pathologic conditions at that point which he has been clearly recognizing for the last fifteen years and which appear almost exclusively in the female, corresponding to lesions, often minimal in size, of the urethrocervical region. These new growths, which appear as small eminences of various degrees, not only may lead to intractable cystitis but may result in grave disturbances of the general health of the patient. Of an inflammatory nature and occurring after prolonged infection of, or toxic effect on, the cervico-urethral mucosa, they may be of enterorenal, staphylococcic or venereal origin. They can be diagnosed only endoscopically and can be recognized as representing any one of five different varieties, namely, polypous, cystic edematous or angiomatous or of the nature of an abscess.

Treatment must be surgical and consists of the application of the high frequency current in the form of etincelage, with the author's forked electrode; this is not a cutting current, nor yet an electrocoagulation, both of which are too drastic. Destruction of each eminence may be supplemented at will by electric curettage of the entire neck of the bladder, if there is pathologic change between the individual outgrowths; but this must be done with the greatest care, with control rigorously maintained at low heat. The results are beyond all expectation; in nearly all cases the patients are entirely cured after two or three months of application. When failure results, it is because the new growths were not the primary cause of the trouble but were the result of a neuro-pathic diathesis.

Rupture.—Dixon and Strohl⁷⁰ reported a case of rupture of the urinary bladder. This case serves to emphasize the importance of surgical intervention in acute abdominal disorders when certain signs, such as acute pain and generalized rigidity, are present. The character of the fluid in the abdominal cavity, although it is no different in appearance than that frequently found in cases in which ascites occurs as a result of a variety of causes, suggested the possibility of urine from a ruptured bladder.

The cause of rupture of the bladder in this case is not known. The patient said that he had voided 3 or 4 ounces (90 to 120 cc.) of urine soon after the onset of the acute pain in the upper part of the abdomen and that he had voided before retiring, eight or nine hours previously.

69. Heitz-Boyer, M.: *La maladie néoformante du col de la vessie chez la femme*, J. d'urol. **42**:216-251 (Sept.) 1936.

70. Dixon, C. F., and Strohl, E. L.: *Spontaneous Rupture of Urinary Bladder*, Am. J. Surg. **33**:110-113 (July) 1936.

The urine obtained by passage of a catheter three or four hours before operation evidently came from the abdominal cavity. The edges of the opening in the bladder were ragged and appeared necrotic. They were trimmed until healthy-appearing tissue was reached. Unfortunately, the excised portion of the wall of the bladder was not preserved for microscopic study. Syphilitic ulcerations do have a tendency to occur in the midline; for instance, ulcerations in the midline of the anterior thoracic wall and sternum are seen occasionally. In such instances syphilis has always to be ruled out as a possible etiologic factor. In this case the rupture was in the midline, and obstruction of the neck of the bladder was not a factor, as it previously has been reported to be in some of the cases.

Incontinence.—Lowsley⁷¹ stated that it is possible to cause rupture of the bladder in animals if the urethra is tied tightly with ribbon gut. Ribbon gut tied around the urethra with moderate tightness will cause stricture and accompanying distention of the bladder and thinning of the wall. If the ribbon gut is applied more loosely, the bladder will succeed in emptying itself against pressure, resulting in marked hypertrophy of the musculature and contraction of the bladder. No hydro-ureter or hydronephrosis resulted from these experiments. The animals were killed or died two months or less after the operation.

In the human being, various muscle transplantations are replaced by the formation of an efficient sphincter by means of ribbon gut, used as an encircling band, a plication suture over the top of the relaxed urethra in the female or as a plication of the membranous urethra in the male. In cases of partial incontinence a cure is effected by encircling the urethra with ribbon gut and tying it snugly. Fibrous tissue replaces the ribbon gut, as was demonstrated by the experiments on animals. The newer plastic operations, made possible by the use of ribbon gut, are more desirable than the older procedures because they make counter-drainage unnecessary, thereby decreasing the period of hospitalization.

Fistulas.—Higgins⁷² reported from a review of the literature that vesico-intestinal fistulas are caused more frequently by an inflammatory process than by carcinoma or trauma. Diverticulitis of the bowel is the most frequent etiologic factor. A preliminary colostomy is advisable in cases in which the causative factor of the formation of fistula is diverticulitis of the colon. The most common sites of the fistulas were between the rectum and the bladder and between the sigmoid and the

71. Lowsley, O. S.: New Operations for the Relief of Incontinence in Both Male and Female, *J. Urol.* **36**:400-413 (Oct.) 1936.

72. Higgins, C. C.: Vesico-Intestinal Fistula, *J. Urol.* **36**:694-706 (Dec.) 1936.

bladder. A diagnosis may be established by cystoscopic and proctoscopic examination and the employment of cystograms and enemas of barium sulfate. Radical operation is essential in dealing with a fistula associated with a malignant growth. Prognosis depends on the etiologic factors associated with the formation of the fistula. Treatment is essentially surgical.

Drainage.—Boyd⁷³ stated that suprapubic cystotomy can be performed with the patient under local and field block anesthesia, which is so much safer for the patient who is a poor risk than any type of general or spinal anesthesia. Suprapubic cystotomy insures a dry wound in practically every case, and if there is any leakage, it is slight and can be controlled readily. It nearly always prevents the development of any except mild infections of the wound. It permits decompression of the bladder and opening the bladder when necessary without distention by air or fluid. It prevents postoperative changes in the symphysis pubis and, as far as can be done, the later separation of the muscles with the formation of hernia. It does not require long experience in operations of the bladder.

The essentials in technic are as follows: A midline incision is made. The fat and fascia from the upper, anterior part of the bladder over an area from 4 to 6 cm. in diameter are freed. The incision in the bladder about the tube is closed with interrupted plain catgut sutures. The bladder is infolded for from 2 to 2.5 cm. with a second layer of sutures. The tube then lies in the middle of the closed incision, and the bladder is not sutured tightly about the tube. The bladder is anchored to the abdominal wall if the capacity of the bladder is large. One large silver wire stay suture is used to approximate the rectus muscles. A small rubber tissue drain passing all the way through the abdominal wall should be left in the upper end of the wound. Closure of the lower 2 to 3 cm. of the wound is not done, and a small piece of fenestrated Dakin tube should be left in that part for drainage.

The postoperative care consists of daily dressings wet with acriflavine and continuous or decompression drainage. The upper and lower ends of the wound are gently opened daily with a hemostat for as many days as necessary to insure adequate drainage.

There were no fatalities in a series of 60 cases, even though some of the patients were very ill, and only 1 had an infected wound. A few superficial, unimportant infections developed about the drains. Thrombosis of the iliac vein occurred in 2 very feeble old men. There have been no hernias or other complications.

73. Boyd, M. L.: Suprapubic Cystotomy for Drainage, *J. Urol.* **36**:740-755 (Dec.) 1936.

PENIS

Tuberculosis.—Lazarus and Rosenthal⁷⁴ reported a case of primary tuberculosis of the penis occurring in a young adult after sexual exposure. Radical amputation of the penis was necessary. This condition is a rare clinical lesion, particularly in adults. Only 25 cases have been reported in the literature to date. The diagnosis is often confused with chancroid, chancre or granuloma inguinale and therefore is made late in the course of the disease. It can be confirmed only by histologic study, preferably by inoculation of an animal. The disease is characterized by a slowly spreading, painful ulcer with an indurated border which has a marked tendency to become undermined and by a central ulceration covered with a yellowish, odorless slough. In the later stages areas of necrosis may be seen near the indurated margin and nodules in the region of the base of the ulcer. The lesion shows a tendency to scar formation, which at times breaks down to form new ulcers and is resistant to all types of treatment. Inguinal adenopathy is generally present but is never an outstanding feature of the disease. Urinary symptoms occur only when the urethra is involved.

In several cases excision or curettage of the lesion associated with the usual hygienic regimen for generalized tuberculosis produced good results. Radical amputation is done in cases in which the glans penis and urethra are extensively involved. The prognosis is favorable in primary tuberculosis of the penis in adults. When it occurs in children after circumcision, the prognosis is unsatisfactory.

URETHRA

Hypospadias.—Walters⁷⁵ stated that the most successful operations for hypospadias have been those in which flaps of skin taken from the penis or scrotum have been used to form a skin-lined canal to the end of the penis from the abnormal opening of the urethra. Operations intended to overcome the penile curvature deformity of hypospadias should be undertaken at a very early age, preferably between 1 and 2 years. Ordinarily this correction can be satisfactorily obtained by means of transverse incisions through the fibrous cord occupying the position of the absent penile urethra, one transverse incision being made immediately in front of the abnormally placed meatus and one relatively far forward close to the glans penis, if a second one is required.

There are three types or degrees of hypospadias: (1) perineal, when the abnormal opening is in the perineum; (2) penoscrotal, when it is

74. Lazarus, J. A., and Rosenthal, A. A.: Primary Tuberculosis of the Penis, *J. Urol.* **35**:361-377 (March) 1936.

75. Walters, Waltman: Successful Operations for Hypospadias, *Ann. Surg.* **103**:949-958 (June) 1936.

at the root or base of the penis, and (3) penile, when it is in the shaft of the penis. The method of Ombrédanne is applicable to all three types of hypospadias and has the advantage that the penile portion of the flap which is used to form the urethra is free from hair. The principles of treatment of hypospadias, as outlined by Ombrédanne, consist in converting a perineal or penoscrotal opening to a penile opening by elevating a longitudinal flap of skin from the scrotum distal to the urethral opening and reflecting it upward; covering it with lateral flaps taken from the adjacent areas of the scrotum.

In the Bucknall operation a delayed flap of skin is raised from the scrotum, forming the anterior portion of the skin-lined canal, which extends from the penoscrotal or penile hypospadiac opening to the end of the penis. Its greatest value is in cases in which other methods have failed, and this is most likely to be in those in which the patients are adults. Healing takes place without the development of a fistula because of the wide attachment of flaps adjacent to the skin-lined canal and the absence of tension on the anastomosis from erections during convalescence, due to the elasticity of the scrotum.

The Thiersch operation in which parallel flaps are taken from the penis gives excellent restoration of the canal unless a fistula develops. It employs tissue free from hair and of fine texture, which is consequently particularly well suited to its changed environment. Unfortunately, it has been characteristic of this type of operation that the formation of a fistula was a relatively common complication, requiring further operations for its repair, oftentimes with unsuccessful results.

Various stages of the Ombrédanne operation have been used, a total of 88 procedures for 32 patients. It was necessary, therefore, in order to obtain a satisfactory end-result to use an average of three stages. The cases were divided about equally into those of perineal, penoscrotal and penile hypospadias. The results in 28 of the 32 cases were excellent. The Bucknall type of operation has been used in 16 cases, and here likewise the operation has of necessity been divided into two stages, to which has been added narrowing of the urethral orifice by the method of Ombrédanne. The results of operation in these cases were excellent. The Thiersch method and its modifications have been used in 13 cases, 46 different procedures being employed in these cases to complete the operation.

Urethral Glands.—Cabot⁷⁶ stressed the conflicting opinions that have existed for a number of years regarding the possibility of lesions of the urethra of the female acting as a focus of infection similar to

76. Cabot, Hugh: Are Glands in the Posterior Urethra of the Female an Important Focus of Infection? *Proc. Staff Meet., Mayo Clin.* 11:589-591 (Sept. 9) 1936.

certain lesions of the prostate and cervix. The evidence in regard to the existence of important glandular structures in the proximal two thirds of the female urethra has been inconclusive.

The conclusion from the recent studies of MacKenzie and Beck⁷⁷ and of Cabot and Shoemaker⁷⁸ on more than 100 specimens removed at postmortem examination was that there are no glandular structures in the proximal two thirds of the female urethra. One of the striking observations in Cabot and Shoemaker's study was the number of very deep crypts in the mucosa, which when seen in cross-section might be mistaken for glandular structures if care were not exercised in studying the arrangement of the cells; these were in fact only simple invaginations of the urethral mucosa.

In the specimens studied a large number of cysts containing albuminous material were found lying beneath the mucosa. According to Cabot, these are the areas which have been referred to by Renner and by Folsom as showing what they regarded as corpora amylacea. The cysts were lined with squamous epithelium and showed no evidence of glandlike structures. They appeared to be entirely similar to the structures seen in the well known conditions of pyelitis, ureteritis and cystitis cystica. In other words, they demonstrated that cystic disease, well recognized in other parts of the urinary tract, is very common in the urethra. Papillary outgrowths in the posterior portion of the urethra were frequently noted. That there are many symptom-producing lesions of the female urethra is an undoubted fact, but the evidence does not warrant assuming that such lesions originate from glands or that they can be made the basis for relapsing infection of the urinary tract in the female. The author expressed the belief that the hypothesis advanced by Renner and by Folsom of a major focus of infection in the posterior part of the urethra of the female comparable with lesions of the prostate of the male has no satisfactory basis in anatomic fact.

Urethral Lymphatics.—Parker⁷⁹ made a study of the lymph vessels from the posterior part of the urethra and stated that the distribution of the lymphatics from this portion and their regional lymph nodes varied for the most part according to the variations in the pelvic arterial branchings.

In 30 stillborn male infants the lymph channels coursed backward along the main pelvic arteries most frequently to nodes situated along

77. MacKenzie, David, and Beck, Sidney: A Histopathologic Study of the Female Urethra, to be published.

78. Cabot and Shoemaker: Unpublished data.

79. Parker, Alice E.: The Lymph Vessels from the Posterior Urethra. Their Regional Lymph Nodes and Relationships to the Main Posterior Abdominal Lymph Channels, *J. Urol.* **36**:538-557 (Nov.) 1936.

the pubic branches of the obturator arteries, to nodes of the internal, middle and external chains of the external iliac groups and to hypogastric nodes, and, occasionally, to lateral sacral nodes, to ischiatic nodes of the gluteal region and to superior hemorrhoidal nodes.

The lymph vessels and nodes draining the postpubic portion of the urethra in the female differed somewhat in distribution from those found in the male. The lymph vessels coursed backward along the umbilical arteries, followed branches and trunks of the hypogastric arteries and traversed the pelvic fascia along the lateral borders of the bladder. The regional nodes for the efferent lymph vessels following those courses were nodes of the internal and middle chains of the external iliac groups, hypogastric nodes, lateral sacral nodes and ischiatic nodes of the gluteal regions.

Indirect and direct connections between lymphatics of the posterior part of the urethra and of the wall of the bladder are described. The courses of extension of injected material from the regional nodes through the posterior abdominal lymph channels to the thoracic duct are illustrated. Some of the lymph nodes, found to be regional or intercalated nodes of the efferent lymph vessels of the posterior part of the urethra, are apparently identical with lymph nodes described in the literature as regional or intercalated nodes for other pelvic organs and regions but were never previously connected with this portion of the urinary tract. Most of the regional nodes for the posterior part of the urethra belong to the principal groups of nodes of the pelvis.

Urethral Tumors.—Campbell and Fein⁸⁰ reported a case of malignant melanoma of the penile urethra which is a clinical novelty and of special pathologic interest. Sarcoma of the urethra most commonly manifests itself by the appearance of a localized neoplasm at some point along the canal. As the growth enlarges, symptoms of obstruction of the lower part of the urinary tract appear. In 4 of the cases reported in the literature a gonorrheal stricture was erroneously believed to be present. With secondary infection of the tumor, the symptoms were suggestive of periurethral abscess, as they were in the case cited by Campbell and Fein. Inguinal adenitis is attributable to metastasis and to lymphatic absorption from the region of the tumor. As the disease progresses, metastasis elsewhere is likely to be noted, even in the cervical region. Ultimately these patients died of neoplastic toxemia or of renal failure.

The diagnosis of tumor of the urethra is suggested by the history of a periurethral swelling in the absence of local infection. The growth

80. Campbell, M. F., and Fein, M. J.: Malignant Melanoma of the Penile Urethra, with a Brief Review of Urethral Sarcoma in the Male, *J. Urol.* **35**: 573-582 (May) 1936.

is usually firm. As in this case, regional metastasis may offer a diagnostic clue. Diagnosis may be confirmed by the histologic examination of a small piece of the tumor removed with a biopsy rongeur introduced through a tubular endoscope. This may be accomplished readily without risk or marked discomfort to the patient. Prognosis is almost uniformly hopeless. Wide excision of the growth offers the only possibility of cure, but because of the high degree of malignancy of these tumors of the urethra and their tendency to metastasize, surgical intervention almost always proves futile. Intensive radiation therapy, either by interstitial implantation or with the roentgen rays, offers the only aid to surgical treatment, but for similar reasons will also fail.

Urethritis.—Gurnee⁸¹ stated that the principles which govern the treatment of gonorrhea in the male should be just as forceful in the female, but because of the absence of pain the tissues are subjected to strong caustics or electric cautery instead of gentle daily manipulation.

Complete shutting off of gonococci results in their death. Curtis has proved this phenomena in tubo-ovarian abscess, and it has been observed to hold true in Bartholinitis; the organism dies in about three weeks if there is no exit for the pus. Incomplete drainage of gonococcic pus results in retarded cures.

By means of the Elliott apparatus a consistently uniform temperature of 128 F. can be maintained for any length of time against a large portion of distended vagina, cervix, adjacent parametrium and pelvic organs, thereby clearing up the latent foci of infection which heretofore were so difficult to reach. Fever therapy with the hot cabinet alone gives only a 55 per cent chance of cure of gonorrhea and is a very drastic treatment. Short wave diathermy, while it gives sufficient heat, is extremely dangerous when used in combination with the hot cabinet for fever therapy. Fever therapy can best be given without any serious complications by combining the hot cabinet and the Elliott treatment.

Owens⁸² considered that by treatment with artificial fever, prompt and dramatic relief of gonococcic arthritis and acute epididymitis can be promised in every instance. Owens stated that this progress in therapy is most appreciated as it applies to arthritis, which was formerly so painful, time consuming and often permanently disabling.

Acute urethritis of less than two weeks' duration has not responded to fever treatment as well as have the chronic infections with prostatic involvement. This experience suggests the possibility that fever therapy

81. Gurnee, W. S.: Gonorrhea in the Adult: Diagnosis; Elliott Treatment and Hyperpyrexia. *Am. J. Surg.* **33**:500-508 (Sept.) 1936.

82. Owens, C. A.: The Value of Fever Therapy for Gonorrhea. *J. A. M. A.* **107**:1942-1945 (Dec. 12) 1936.

alone should not receive all the credit for the apparent cures and that natural resistance in the cases of acute infection has not yet developed the antigenic factors that are probably more active in the cases of chronic infection.

Clinical experience is accumulating to support the laboratory conclusions that certain strains of gonococci may be utterly destroyed by temperature of a degree and duration tolerable to the patient, while other strains are resistant to such temperatures. An increasing number of patients have achieved apparent cure after a single session of six hours at a temperature of 106.5 F., while others receive no appreciable benefit after four sessions.

Given patients who can and will take the treatment, more than 80 per cent of gonococcic infections regardless of complications may be absolutely cured in two weeks. Ability of the patient to take the treatment depends on the condition of the heart, the resistance of the skin to heating and the patient's temperament. Those who are unsuitable for one reason or another constitute 12 per cent in Owens' series.

Urethral Injury.—O'Connor⁸³ stated that in a period of thirteen years he treated 31 men suffering from traumatic rupture of the urethra. Eight incurred this injury from falling astride a loose man-hole cover. He stated that although no mention of injury from this source is to be found in the textbooks, personal inquiry has disclosed that in the larger metropolitan centers it occurs sufficiently often to deserve comment. The blow received by the perineum is especially severe, because the metal cover is swung violently upward and strikes as the body is lurching downward and forward. In the 8 patients so injured, the posterior bulbous urethra, close to the triangular ligament, received the impact. In none was the pelvis or other bones fractured. When the urethral floor is so severely traumatized that continuity is destroyed, the proximal (vesical) portion is retracted and elevated by the pull of the strong fascial attachments to the urogenital diaphragm. The extent of the separation of the torn urethral edges depends largely on whether the floor of the urethra is severed or whether the roof alone is torn across. If the floor alone is injured and the roof of the urethra is intact, one may be fortunate enough to guide a small, soft rubber catheter (Wishard), passed over a fairly rigid stylet, by careful and close adherence to the roof of the urethra during the insertion. When this procedure is successful, drainage of the bladder is supplied by the indwelling catheter, and unless there has been perineal extravasa-

83. O'Connor, V. J.: Repair of Rupture of the Male Urethra, with Report of Eight Injuries from Falling Astride a Manhole Cover, *Surg., Gynec. & Obst.* 63:198-200 (Aug.) 1936.

tion or marked hemorrhage, no incision is necessary. If perineal extravasation or hemorrhage has occurred, single or multiple incisions in the perineum with adequate provision for drainage will suffice, and the urethral lumen will restore itself along the indwelling catheter.

Except in instances of crushing injury of the floor of the urethra without separation of the urethra at the point of injury, catheterization, even carefully and expertly done, is rarely possible. It should be emphasized that repeated unsuccessful attempts at catheterization only increase the local injury and add to the dangers of increased hemorrhage and deep-seated infection.

In all cases of rupture of the urethra from external violence, the ease of repair and the rapidity of recovery depend largely on the avoidance of unsuccessful catheterization and the recognition of the necessity for immediate surgical intervention.

Until recently O'Connor favored the perineal approach in draining the bladder and in attempting properly to restore the urethral lumen. Although patients so treated did well and usually enjoyed a somewhat shorter period of hospitalization than those treated suprapubically, the resultant perineal and urethral scarring was always considerable and necessitated frequent and repeated urethral dilation for a prolonged period. The method now preferred is extraperitoneal cystotomy, with retrograde splinting of the urethra by an indwelling catheter and perineal incision only when necessary to drain extravasated blood and urine. This splinting is accomplished by the use of interlocking sounds which are passed simultaneously through the posterior and the anterior part of the urethra and joined in such a way that the urethral sound may be guided safely into the bladder. A no. 22 French soft rubber catheter is then stitched securely over the end of the urethral sound and withdrawn through the urethra. The catheter is properly fixed in the urethra, and the bladder is closed in the usual manner with a small mushroom catheter in the dome for immediate drainage. The urethral catheter is closed for a period of from five to seven days, suprapubic drainage being allowed during this time. The urethral catheter is then opened, the bladder is irrigated and the suprapubic tube is removed. There is rarely any suprapubic leakage of urine after this time, as drainage is adequately supplied through the urethral catheter. This is removed when the suprapubic wound seems firmly healed, usually on the twelfth to the sixteenth day after operation. The complete restoration of normal urinary function and the subsequent lack of urethral stricture are the obvious advantages of this method. These patients require occasional urethral dilation, to be sure, but they do not present the serious problem of potential stricture that is almost invariably present after perineal urethrotomy.

TESTIS

Ectopia.—Deming,⁸⁴ after a series of experiments with monkeys, stated that the gonadotropic factor is a definite aid preceding and following surgical treatment of the undescended testis. It enlarges the inguinal canal and the cord and renders the testis more movable in the monkey. Treatment may be instituted in the human being as early as 2 years of age. The earlier the treatment the better are the chances for a normally functioning testis. The histologic picture in the monkey six weeks after the cessation of the administration of the gonadotropic factor persists with negligible change.

Woodruff and Milbert⁸⁵ reported a case of strangulation of an undescended testis by a loop of omentum. It represents a rare and previously unrecorded complication threatening the safety of the maldescended organ. Etiology, pathology, symptomatology, diagnosis and treatment are discussed as they pertain to the condition in question. In this instance it is rather ironical that the omentum, so frequently referred to as the "policeman of the peritoneal cavity," should have wandered astray to become the "hangman" of the testis.

Cysts.—Abell⁸⁶ reviewed cysts of the testis, excluding hydroceles of the tunica vaginalis, encysted hydroceles of the cord and those occasionally noted in the body of the testis proper; they arise within epididymal structures or vestigial remnants connected with them. Abell observed 32 instances of cysts conforming to this in origin and site.

Four patients gave a history of trauma with the appearance of the tumor immediately thereafter. One other stated that the tumor appeared after the wearing of a truss and still another that it developed after an operation for hernia.

The size was noted in 26 cases; the smallest tumor was 1 inch (2.5 cm.) in diameter, and the largest measured 8 by 4 by 4 inches (20 by 10 by 10 cm.); the size of the remainder varied between these limits. Twenty-five of the 32 patients came to operation, the character of the growth being unilocular in 12 cases, multilocular in 9 and polycystic in 4; 21 were unilateral and 4 were bilateral; 3 were enclosed within the tunica vaginalis or were intravaginal, and 22 were extravaginal. Twenty-six operations were done on 25 patients, 1 patient returning after fourteen years with recurrence of the cyst in the site of the former operation.

84. Deming, C. L.: The Gonadotropic Factor as an Aid to Surgery in the Treatment of the Undescended Testicle, *J. Urol.* **36**:274-288 (Sept.) 1936.

85. Woodruff, S. R., and Milbert, A. H.: Strangulation of the Undescended Testicle by a Loop of Omentum, *J. Urol.* **36**:558-563 (Nov.) 1936.

86. Abell, Irvin: Cysts of the Testicle, *Ann. Surg.* **103**:941-948 (June) 1936.

The pathologic report revealed polycystic disease in 4 cases, which was bilateral in 2 and unilateral in 2. Specimens from 1 case of bilateral polycystic disease were unusually large, measuring 170 by 60 by 40 mm. and 150 by 50 by 30 mm., respectively. Of the specimens from the cases of bilateral involvement, only 1 showed recognizable epididymal tubules, being composed of pale pinkish gray fibrous and serous tissue containing many simple thin-walled cysts clumped together in masses. The cysts varied in size, measuring from 2 to 40 mm. in diameter, and contained clear, colorless fluid. The unilateral specimens were similar in character. In some of the cysts the walls were hyalinized and vascularized and revealed lymphocytic infiltration.

These cysts may be considered as falling in three groups: (1) cysts having their origin in vestigial remnants, (2) retention cysts and (3) polycystic growths or cystic embryomas.

URINARY CALCULI

Gray⁸⁷ reported a series of clinical cases of stone in the urinary tract from the Lester Chinese Hospital in Shanghai. He stated that infection played little part in the etiology and that it certainly is not an essential feature. The reaction of the urine has also not been of great significance. In the experimental cases, although the tendency has been for the urine to become alkaline, stone may form before this happens.

The two positive findings which have been observed throughout the study have been: (1) some alteration in the metabolism, so that the urine may be considered to be supersaturated with stone-forming substances and the formation of sediment would therefore be likely, and (2) a local factor in the urinary tract. It is felt that the latter probably acts by altering in some way the colloid conditions, so that the sediment becomes a concrement. It is suggested that in most cases this factor has been some alteration in the integrity of the epithelial lining of the tract. Such a change may easily be produced experimentally by trauma, obstruction, perhaps infection, devitalization by means of injury to the vascular supply, chemical irritation and a diet deficient in vitamin A. The last-named factor needs to be of a severe grade, but if it is it will produce a series of changes of which the last stage is keratinization. Formation of stone may occur in the presence of either of these factors singly, but much more readily in the case of the second. In the clinical cases it is felt that such alterations in the epithelium might well occur, and a number of biopsies of the mucosa of the bladder have been made. With the exception of 2 cases, however, although changes have been noted, they have not approached the

87. Gray, J.: Urinary Stone Formation, Clinical and Experimental, Chinese M. J. 50:761-786 (June) 1936.

severity of those obtained by experimental means, especially by the diet deficient in vitamin A. Neither has there been any other evidence in a survey of the diet or in the clinical condition of the patients to suggest more than at most a slight deficiency in vitamin A. However, it was shown experimentally that with the diet stone may form before the epithelial change has progressed as far as as keratinization. This was particularly true if an excessive quantity of vitamin D had been added to the diet.

As a large number of the patients have been children or members of the laboring class who work in the open without many clothes, it was felt that the possibility of a moderate excess of absorption of vitamin D must be considered, or perhaps a combined deficiency of vitamin A with an excess of vitamin D. Apart from this, although the number of clinical cases investigated is not yet large enough, the evidence does not point strongly to a deficiency of vitamin A of any severe grade.

The effect of polishing rice, particularly in regard to the possibility of calcium dust being mixed with the food, is felt to be of importance in Eastern countries.

Hou,⁸⁸ in his experiments on albino rats, showed that the addition of vitamin D to a diet which was deficient in vitamin A and in fat increased the incidence of urinary calculi and the removal of vitamin D decreased it. Alteration of the protein content of the diet also affected the frequency of formation of urinary calculi. Both a high and a low casein content resulted in an increase in the number of cases of calculi up to 100 per cent. Chemical analysis of the proteins for calcium and phosphorus indicated that the result was not due to an unbalanced calcium and phosphorus ratio. A lowering of the inorganic calcium and phosphorus in the diet caused an increase of the incidence of urinary calculi. The addition of heated lard caused a decrease in the frequency of calculi. Rats on the diet low in calcium and phosphorus, however, showed an increase.

In general, among the different groups studied the occurrence of calculi appears to run parallel to the presence of infection or of severe changes in the epithelium of the kidney and the urinary bladder. The presence of calculi in the kidney or in the bladder bears some definite relation to the type of diet used.

The calculi found in the various groups studied consisted mainly of triple phosphates.

Snapper, Bendien and Polak⁸⁹ stated that urine contains many salts and compounds in solution, some of which are hardly water

88. Hou, H. C.: The Influence of Diet on the Formation of Urinary Calculi, *Chinese M. J.* **50**:787-796 (June) 1936.

89. Snapper, I.; Bendien, W. M., and Polak, A.: Observations on the Formation and the Prevention of Calculi, *Brit. J. Urol.* **8**:337-345 (Dec.) 1936.

soluble, such as uric acid and calcium oxalate. This condition is brought about by two factors: (1) the hydrotrophic action of certain substances, such as urea and hippuric, salicylic and mandelic acids, which further the solubility of insoluble salts, and (2) the presence of colloids. For example, 100 cc. of water will dissolve 0.63 mg. of calcium oxalate, while 100 cc. of a 3 per cent solution of urea will dissolve 1.28 mg. Likewise 100 cc. of water will dissolve 0.8 mg. of calcium carbonate, while a like amount of 15 per cent sodium salicylate will dissolve 5 mg. The benzoates, hippurates and mandelates have the same property.

In the development and growth of renal stones, precipitation of flocculation of the colloids which form the nucleus and frame of the stone is more important than the precipitation of salts, which is secondary. Therefore, calculogenesis and growth may be inhibited by stabilizing the urinary colloids; without precipitation of the colloids no renal stone can develop or increase in size. The authors have shown that *in vitro* the salicylates will prevent precipitation of different colloids by aluminum sulfate, and that other salts, such as the hippurates, the benzoates and the mandelates, are less effective in this respect. Because hippuric acid has the property of hydrotrophy and also inhibits flocculation of colloids, the authors considered that its presence in the urine assumes new importance.

In experimental calculus brought about by the use of a standard diet with vitamin A but with large amounts of calcium carbonates (3 per cent) they prevented the formation of stones by the use of large amounts of sodium benzoate, which is excreted in the urine linked with amino-acetic acid as hippuric acid. They also cleared up clinical phosphaturia without changing the reaction of the urine by giving 6 Gm. of sodium benzoate daily. They attributed this to the hydrotropic property of hippuric acid and concluded that the use of this substance is a rational measure in preventing recurrent calculi. Hippuric acid was used because it is a physiologic constituent of the urine. Other stabilizing and hydrotropic substances, such as the salicylates and mandelates, may give even better results.

Kretschmer⁹⁰ reported that of 21 children with stone in the urinary tract, 4 did not undergo treatment. Three of these passed stones spontaneously. The fourth was a girl with a large stone in the kidney, for which surgical intervention was advised but was refused.

In 5 cases stone was removed from the kidney by pyelolithotomy and in 1 by nephrolithotomy; in 2 cases resection of the kidney was also carried out. The patients with stone in the ureter were treated by

90. Kretschmer, H. L.: Stone in the Urinary Tract in Children: A Critical Study of Twenty-One Cases, *Ann. J. Dis. Child.* 52:513-527 (Sept.) 1936.

ureterotomy. Five of the patients with stone in the bladder were treated by suprapubic lithotomy, and 5, by litholapaxy. There were no deaths and no postoperative complications.

The indications for the treatment are the same in the child as in the adult. If the stones are small enough to pass, if they produce only slight evidence of obstruction or none at all and if infection is mild or absent, medicinal management is justifiable, that is, the administration alternately of urinary antiseptics and alkaline diuretics. The child should be encouraged to drink large quantities of water, milk, lemonade and other liquids. When the stone in the kidney or the ureter is large, so that it produces definite obstruction, or when there is profuse blood, infection or repeated attacks of renal colic, the patient should be operated on.

SURGICAL TREATMENT FOR UROLOGIC CONDITIONS

Priestley and Counseller⁹¹ stated that during 1935 there were 764 patients with urologic conditions on whom 917 operations were performed. These 917 operations included 1,555 surgical procedures. There were 14 deaths in the entire group, or a mortality of 1.8 per cent of the total patients operated on. Hydronephrosis, nephrolithiasis and tumors constituted most of the conditions for which operation was performed. Included in this group were certain patients with far advanced disease. Conservative surgical procedures in selected cases of hydronephrosis are now fairly well standardized and yield satisfactory results in the majority of cases. Nephrolithiasis is a condition which still presents many problems, especially regarding etiology and the prevention of recurrence. In this series 32 renal tumors were removed without a death. Some very large neoplasms were extirpated satisfactorily after preliminary roentgen therapy. Occasionally the anterior approach to the kidney was employed.

Of 57 patients with ureteral lithiasis, transurethral manipulation of the stone or stones was performed on 44 per cent and ureterolithotomy on the remainder. Rather definite indications exist for each procedure, and the best results are obtained by judicious selection of patients for each method. Transplantation of one or both ureters to the sigmoid colon was performed on 13 patients because of various lesions of the bladder, with 2 deaths. Three patients were subjected to transplantation of one or both ureters to the skin with complete recovery.

Forty-two patients underwent suprapubic operations on the bladder, with 2 deaths. Twenty-seven of the 42 patients were suffering from carcinoma of the bladder. It is interesting to note that total cystectomy

91. Priestley, J. T., and Counseller, V. S.: Review of Urologic Surgery for 1935, Proc. Staff Meet., Mayo Clin. 11:801-804 (Dec. 16) 1936.

for carcinoma was performed on 4 patients without a death. During 1935, 695 patients were subjected to transurethral resection of the prostate gland, whereas prostatectomy was performed on only 2. Cystostomy as a procedure preliminary to transurethral resection was performed on only 3 patients.

A total of 865 surgical procedures were performed on the external genitalia. In many instances multiple surgical procedures were performed on a single patient, especially for certain congenital anomalies which required plastic repair. The surgical treatment of undescended testes gives good results in the majority of cases, whereas experience with the hormonal treatment of this condition has not been so uniformly successful. Determinations of the gonadotropic substance in the urine have been of value in the treatment of patients who have testicular tumors, especially during the postoperative period. The authors trust that the ensuing year will settle some of the existing problems in this field of surgery and open new fields for further advances.

Seventy patients who had carcinoma of the bladder underwent treatment last year. Thirty-three per cent were treated by the suprapubic approach only. In 4 the urine was diverted above the bladder, in 3 by ureterosigmoidal anastomosis and in 1 by bilateral ureterostomy, followed by total cystectomy, without the death of any patient. Cabot has shown previously the simplicity of the technic used in performing bilateral ureterostomy and the low surgical risk. It should be possible, therefore, in treatment of some of the more advanced lesions, to perform bilateral ureterostomy and later total cystectomy and to follow these procedures by radium therapy.

By the methods used today, when preparing a patient for operation on the colon by means of injections of vaccines intraperitoneally, cleansing the bowel and special diets, it is possible in a greater number of cases successfully to transplant the ureters to the sigmoid colon and later to perform the radical operation of removal of the involved bladder.

Whenever a ureter is dilated and the walls are thickened by infection, ureterosigmoidal anastomosis should not be considered. In such cases cutaneous ureterostomy is the operation of choice. One other fact that militates against radical removal of the bladder and diversion of the urinary stream in many cases in which the lesion is of a high grade of malignancy is that metastasis to the regional lymph nodes has been discovered oftener than previously was suspected.

TRANSURETHRAL MANIPULATION

Thompson⁹² stated that before the advent of the resectoscope the complete destruction of an epithelioma of the bladder of a diameter much

92. Thompson, G. J.: *Transurethral Operations: Changing Conceptions During the Past Five Years*, J. A. M. A. **107**:1954-1958 (Dec. 12) 1936.

greater than 1 cm. involved repeated electrocoagulation of the growth at intervals of from a week to a month. The cutting loop of the resectoscope has been found to be a satisfactory instrument for the rapid removal of many tumors of a pedunculate or relatively noninfiltrating type. The bulk of the growth can be rapidly removed with the cutting current, after which the pedicle or base can be thoroughly destroyed by electrocoagulation.

In some cases, particularly in those in which microscopic study reveals a high grade of malignancy, it is well after removal of the tumor to implant radon seeds in the underlying wall of the bladder. In certain cases in which the extent of the lesion or the general condition of the patient has precluded radical surgical removal, this method, combined with subsequent roentgen therapy, has resulted in remarkable palliation, and in some instances it apparently has resulted in a cure.

At the Mayo Clinic during the period from 1932 to 1935 inclusive, tumors have been destroyed in 191 cases by the methods outlined, practically always at one sitting. The results to date from such treatment have been gratifying, on the whole, although sufficient time has not elapsed to warrant final conclusions concerning the efficacy of the method.

Litholapaxy has been advocated for many years for the removal of calculi in the urinary bladder. The presence of a considerably hypertrophied prostate gland was always deemed a contraindication to litholapaxy. Thompson has previously reported a series of cases in which he was able to crush and remove large calculi and, using the same anesthetic, to resect the obstructing portion of the prostate gland. The greatest amount of tissue removed in any case was 47 Gm. It is important that litholapaxy be performed rapidly; hence a lithotrite of the Bigelow type is used by preference. As a general rule it is best to crush the stone prior to prostatic resection, but if the lithotrite cannot be passed easily beyond the prostatic enlargement, it may be necessary to perform prostatic resection first. During the past four years 161 patients with vesical calculi have been treated by conservative transurethral methods at the Mayo Clinic.

Bumpus and Thompson in 1930 reported on a clinical study of 1,001 cases of ureteral calculi; in 60.7 per cent of cases in which a calculus occurred in the lower part of the ureter it was removed by transurethral methods. In most of the cases in that series more than one attempt was made before the stone was obtained, and many times it was not passed until a number of days subsequent to manipulation. During the years 1932 to 1935 inclusive, stones have been removed from the ureter by transurethral methods in 180 cases at the Mayo Clinic; in the large majority of cases the first attempt was successful, the calculus being

removed at the time of the operation, either by engagement with an extractor or by the safer method of enmeshing it with multiple catheters. An attempt to force an extractor into a small ureter may result in perforation and certainly will cause severe reaction. One should prefer to insert two or three catheters alongside the stone and leave them in place for from forty-eight to seventy-two hours. Twisting the catheters at that time will often be more profitable than doing so immediately after they are placed.

Prostatic calculi often do not produce symptoms. Hence, Thompson has practically always disregarded their chance finding by routine roentgenographic study. However, when either for local or for focal reasons it is essential to reduce or eliminate the prostatitis which generally is found in association with prostatic calculi, it is not a difficult task to remove the stones by transurethral incision. Thompson prefers to use the Collings knife, for one can gage the depth of the incision, making it no deeper than is actually necessary to expose the nests of stones. Such operations must always be done with thorough recognition of the fact that the procedure is a minor one as far as the patient is concerned but that lack of caution on the part of the surgeon may easily result in a major complication, if not in death. In 8 cases Thompson has incised acute prostatic abscesses with the Collings knife, thus evacuating a large pocket of pus through the urethra.

There has been no mortality from any of the transurethral procedures described, except in the form of cases in which prostatic resection was performed. Of 1,987 patients subjected to transurethral resection for either benign or malignant involvement of the prostate gland during the years 1932 to 1935 inclusive, only 14 died, a mortality of 0.70 per cent.

INFECTION OF THE URINARY TRACT

Frisch⁹³ reported 47 cases of pyelitis due to colon bacillus in which bacteriophage was employed therapeutically, in all of which the condition had proved resistant to other methods of treatment. The lysin was injected into the renal pelvis, and in 2 children a subcutaneous injection was made also. The method of preparation and administration of the bacteriophage is described.

In 30 of the 47 cases cure was effected, and the urine was sterile after the treatment. In 6, there was improvement. In 6 cases the colon bacillus was resistant to the lysin during the treatment, and in these cases improvement did not occur. Five of the patients discontinued treatment before being cured.

93. Frisch, Bruno: Ueber das Phänomen der Bakteriophagie in der Urologie, *Ztschr. f. urol. Chir. u. Gynäk.* 42:199-205, 1936.

Frisch considered bacteriophage a valuable adjunct to other methods of treatment.

Cook⁹⁴ stated that during recent years urologists have realized the value of a most careful bacteriologic investigation of the urine in cases in which infection is suspected. The simple Gram stain of urinary sediment, supplemented by culture of the urine, usually yields information of the greatest value in arriving at the proper diagnosis and is also of value in suggesting the best method of treatment. Repeated examinations are frequently necessary, especially in cases of coccic infection. It is emphasized that one organism may completely check the growth of another, the second organism coming into prominence only after the first has been partially or completely destroyed. The more common infections of the urinary tract, excluding tuberculosis, can be divided into two main groups, namely, those produced by a bacillus and those produced by a coccus. Cook is concerned with a third group of cases, however, in which no organisms can be found even after careful study. He referred to a group of patients who have definite urinary symptoms and who respond to the ordinary methods of treatment of infection in the urinary tract, but positive cultures of the urine are never obtained, although various degrees of pyuria are present. In these cases it is of prime importance to exclude tuberculosis. This is accomplished by the use of cystoscopy, urographic data, repeated examinations for acid-fast bacilli and inoculations of guinea-pigs with urine from the bladder and kidneys. The etiology of this group of cases in which specific organisms cannot be found is obscure. Almost invariably the disease has been present for months or even years, and local symptoms are well marked. Frequent urographic examinations suggest inflammation of long standing. Results of treatment, however, are ordinarily gratifying if renal function remains satisfactory. It may be necessary to continue treatment over a period of from six to eight weeks before improvement is noted. At the beginning treatment consists of lavage of the bladder with potassium permanganate (1:8,000) alternating with a solution of acetic acid (1:3,000) and followed by the instillation of silver iodide. The ketogenic diet is usually employed aided by acidification of the urine by the administration of ammonium nitrate or ammonium chloride in doses of 6 Gm. daily, if necessary, on the third or fourth day of the diet. Intravenous injections of neoarsphenamine are given at intervals of five days until from two to four injections have been administered. Careful search for foci, with eradication of these when present, is perhaps one of the most important factors in treatment. This includes

94. Cook, E. N.: Infections of the Urinary Tract of Obscure Etiology, *J. Urol.* **36**:460-466 (Oct.) 1936.

investigation of the teeth, tonsils, prostate gland and cervix uteri. The author reported 4 illustrative cases in detail. It is emphasized that no single method of treatment has been uniformly satisfactory and that a combination of all forms of treatment considered has ordinarily yielded the best results. It seems that this group of cases represents a definite clinical entity.

Dillon⁹⁵ stated that foci of infection play an important part in the causation of infections of the urinary tract. In vague septic conditions more attention must be paid the urinary tract as a possible site of infection, in spite of negative results of clinical examination of the urine. Dentists should be taught to recognize more of the medical and surgical aspects of an infected alveolar process. Before condemning the patient with symptoms referable to the bladder and "clear urine" as neurotic, larger quantities of urine from the bladder should be sent to the bacteriologist with the request that the examination be made on the concentrated sediment of the entire specimen. Children should be watched more closely during the tooth-cutting age and attention given to dental care and hygiene. Also, during septic reactions the urinary tract should not be forgotten, and more exacting examinations should be made for the presence of bacteria in the clear urine.

URINARY ANTISEPTICS

Cook and Buchtel⁹⁶ in the past nine months have given mandelic acid to more than 250 patients. Early results indicated that it was effective in approximately 50 per cent of cases, but more recently, with more careful management, the percentage of good results has been greatly increased. For the most part sodium mandelate in a 10 per cent solution was used. A dose of 1 ounce (30 cc.) before each meal and at bed time was employed, and an acidifying drug, such as ammonium nitrate or ammonium chloride, was usually given. The intake of fluid was reduced to 1,200 cc. daily. In a series of 75 cases in which this drug was employed the urine became sterile in 61 cases, or 81 per cent. In attempting to obtain the desired acidity of the urine without the use of an additional acidifying drug, ammonium mandelate has been satisfactorily employed, following the suggestion of Holling and Platt. Only 1 patient in 15 required a secondary acidifying drug. In order to obtain the best results extreme care and alertness must be used in managing this form of treatment. The urinary p_H must remain below 5.5. Occasionally it will be necessary to employ dietary measures in addition to

95. Dillon, J. R.: Urinary Tract Infection with "Clear Urine," California & West. Med. 45:489-491 (Dec.) 1936.

96. Cook, E. N., and Buchtel, H. A.: The Use of Mandelic Acid for Infections of the Urinary Tract, Proc. Staff Meet., Mayo Clin. 11:538-540 (Aug. 19) 1936.

acidifying drugs in order to obtain the desired urinary p_H . In certain cases mandelic acid has been used in conjunction with a ketogenic diet with satisfactory results. To the present time this drug seems to be the most useful in treating bacillary infections and can be used in cases of gout, duodenal ulcer or diabetes mellitus with much less risk than the ketogenic diet. The authors stated that care should be utilized in administering the drug to aged patients or if renal function has been reduced, as it may cause a temporary detrimental effect on renal function. Less than 1 per cent of the patients complained of nausea or vomiting while mandelic acid was being administered. About 10 per cent complained of mild diarrhea, although occasionally the diarrhea was so severe that it was necessary to cease administration of the drug.

Cook,⁹⁷ because of certain unpleasant reactions and unsatisfactory results in the treatment of infections in the urinary tract by means of the ketogenic diet, has endeavored to find an adjunct to this method of treatment which will enhance the efficacy and alleviate the distressing complications. Fuller has demonstrated that the product necessary in the urine of patients on a ketogenic diet to render the urine bactericidal is beta-hydroxybutyric acid. Fuller suggested the use of this substance by mouth and recorded a small increase in the beta-hydroxybutyric acid content of the urine after the oral administration of 1 Gm. of this substance three times a day. This suggested the possibility of the oral, intravenous and local use of this substance as an adjunct to ketosis.

The oral administration of synthetic racemic beta-hydroxybutyric acid will definitely increase the urinary excretion of this substance when the patient to whom the drug is given is in a state of sufficient ketosis. There is no effect when the substance is given to a patient who displays little or no ketosis.

The local use of a 2 per cent solution of beta-hydroxybutyric acid buffered to a p_H of from 4.4 to 4.5 has proved beneficial in those cases in which the results with the diet have been unsuccessful or in which the patient has been unable to stand the dietary regimen. Seven of the 10 patients so treated gave negative urinary cultures. In 2 of the remaining 3 patients, symptoms were markedly relieved, while 1 patient obtained no benefit.

The sodium salt of beta-hydroxybutyric acid, when given orally, will produce an increase in urinary excretion of the acid but apparently to a less degree than oral administration of the pure acid.

97. Cook, E. N.: The Use of Beta-Hydroxybutyric Acid and Certain of Its Salts as an Adjunct in the Treatment of Infections of the Urinary Tract. *J. Urol.* 36:289-297 (Sept.) 1936.

The calcium salt of the beta-hydroxybutyric acid was given intravenously in 3 cases. In none of these was an appreciable change noted in the urinary concentration of the acid.

Helmholz and Osterberg⁹⁸ recalled that they previously presented data to show that oxybutyric acid appears in the urine as the result of incomplete combustion of fats when only small amounts of carbohydrate are given in the diet. This so-called ketogenic diet is difficult for many patients to take. Recent work, originating with Rosenheim in England, has demonstrated that mandelic acid when taken orally escapes metabolism or conjugation in the animal organism and is excreted in the urine by the kidney in a concentration sufficient for bactericidal action, provided the p_H of the urine is lowered simultaneously. In man, after the oral ingestion of 5 Gm. of sodium mandelate in one dose, 80 per cent of the ingested mandelic acid appears in the urine within twenty-four hours, and the maximal excretion occurs approximately two hours after ingestion. When 3 Gm. of mandelic acid in the form of a 10 per cent solution of sodium salt is given four times during the day, there is a cumulative excretion of the acid as various quantities are ingested, and although diuresis may be produced, the concentration of the acid reaches a value in excess of 1 per cent. By administering ammonium chloride and mandelic acid together, the p_H of the urine can be lowered to approximately 5.0 over a period of many days, while a concentration of 1 per cent mandelic acid is maintained in the urine. These values have been shown to be most effective in sterilizing the urine. If from 0.25 to 1 per cent mandelic acid can be maintained in the urine, the acid will act bactericidally on most organisms at a p_H ranging from 5.0 to 5.7. Certain strains of *Aerobacter* and *Pseudomonas* are far more difficult to kill than is *Escherichia coli*.

Carroll, Lewis and Kappel⁹⁹ reported a clinical experience with 50 cases of pyuria in which mandelic acid was administered as suggested by Rosenheim. An analysis of their results shows 37 cases of infection due to the colon bacillus, including acute and chronic pyelitis, pyelonephritis, diverticulum of the bladder, nephroptosis, renal calculi, prostatic hypertrophy with retention and cystitis. In all these, the urine became microscopically clear under the treatment. In 7 cases the urine yielded positive cultures. The average number of days of treatment required to produce sterile urine was seven. Although the condition of 7 patients with coccic infections improved, the urine did not become

98. Helmholz, H. F., and Osterberg, A. E.: Rate of Excretion and Bactericidal Power of Mandelic Acid in the Urine, *J. A. M. A.* **107**:1794-1796 (Nov. 28) 1936.

99. Carroll, Grayson; Lewis, Bransford, and Kappel, Louis: Mandelic Acid as a Urinary Antiseptic: A Clinical Study, *J. A. M. A.* **107**:1796-1799 (Nov. 28) 1936.

sterile. In only 1 of 6 cases of infection due to *Bacillus proteus* was the urine made sterile. The proteus organism is the most resistant to elimination from the urinary tract. In 81 per cent of all cases of colon bacillus infection in which this manner of treatment was employed, the urine was sterile. The authors concluded from this survey that a urinary infection due to the colon bacillus group in which a p_H of 5.5 is maintained may be expected to clear up with the administration of mandelic acid within from four to twelve days. They further emphasized that pyuria is only a symptom and that complete urologic examination should always precede therapy with mandelic acid. The original causative factor in producing the pyuria must be recognized and treated together with the administration of the acid. Caution must be exercised in giving the proper dosage for fear of poisoning. Persons with lowered renal function should not be given mandelic acid.

URINARY EXTRAVASATION

Char, Shih and Yang¹⁰⁰ reported 30 cases of extravasation of urine from the Peiping Union Medical College Hospital. They stated that the most common cause of extravasation of urine is a urethral stricture caused by gonorrheal infection. The urethra proximal to the stricture gradually becomes dilated and weakened because of increased pressure and secondary infection. Rupture eventually occurs with escape of urine into the adjacent tissues. The next cause in order of frequency is trauma to the perineum or a fall astride a hard object. In 3 cases a stone was found in the urethra. The extravasation in these cases apparently was not caused by a stricture but by obstruction attributable to the stone. Occasionally in cases of severe phimosis of long duration, when the preputial opening has been reduced to the size of a pinpoint, extravasation may take place through ulceration of the inner surface of the prepuce. In such cases the urine will extravasate first into the penis and then into the scrotum.

The clinical picture of extravasation of urine is determined principally by the situation of the extravasation, the rapidity with which it occurs and the virulence of the invading organism. If extravasation is rapid, as in the case of a direct injury to the perineum or a fall astride a sharp object resulting in complete division of the urethra, the presenting symptoms will be sharp pain at the site of the injury, bleeding from the urethra, swelling in the perineum and inability to urinate.

Since extravasation is an urgent condition, treatment should be instituted as soon as possible. The treatment should aim to overcome

100. Char, G. Y.; Shih, H. E., and Yang, C. P.: Extravasation of Urine. Chinese M. J. 50:807-820 (June) 1936.

uremia, to provide adequate drainage and to release the stricture or repair the injury to the urethra.

Seven patients in this series died in the hospital, giving a mortality of 23 per cent. Two patients left the hospital against advice and died shortly afterward. If all the fatal cases were considered together, the mortality would amount to 30 per cent. Eight of the 9 fatal cases were from the group of cases of gonorrheal stricture, and in only 1 of these cases did death follow traumatic injury of the urethra. The deaths were mainly attributable to three factors: 1. The patients came late for treatment when the degree of acidosis and uremia was extreme. 2. The extravasation was extensive and complicated by infection by virulent organisms. 3. The distended urinary bladder was probably emptied too suddenly at the time of operation.

Negley¹⁰¹ stated that the mortality from urinary extravasation is unbelievably high in persons after the age of 40. The duration of the disease is an important factor in determining the prognosis. The longer extravasation occurs, the more virulent is the infection and the less chance for recovery. Cystotomy, with incision and drainage, seems to be the operation of choice and carries the lowest mortality. Bisection of the scrotum seems in some way to detract from chance of recovery and to add to the mortality unless accompanied by other incisional drainage. The causes of death in order of frequency are septic toxemia, pyelonephritis and cardiac failure, and in most cases degeneration of kidneys, liver and spleen is associated. Periurethral, scrotal, penile, abdominal and phlegmonous processes may occur without urinary extravasation and may be entirely bacterial with exudate.

DIVERSION OF URINARY STREAM

Cabot¹⁰² discussed the three common procedures for diverting the urine above the level of the bladder, namely, nephrostomy or pyelostomy, uretero-enterostomy and cutaneous ureterostomy. The general indications, technic and postoperative care for each procedure are considered.

Nephrostomy seems preferable to pyelostomy, except for temporary drainage, because it is more effective. Drainage is more complete and continuous and there is no leakage. Furthermore, displacement of the tube is more readily avoided, and if necessary nephrostomy may be utilized as a method for permanent drainage. Properly performed nephrostomy does not involve significant injury to the renal parenchyma.

101. Negley, J. C.: Urinary Extravasation, *California & West. Med.* **45**:38-41 (July) 1936.

102. Cabot, Hugh: The Methods of Diverting Urine Above the Level of the Bladder, with Particular Reference to Problems of Technic, *J. Urol.* **35**:596-609 (June) 1936.

A fistula after nephrostomy is practically unknown, whereas it occurs more frequently after prolonged drainage by pyelostomy. The author discussed several different technics for performing nephrostomy and suggested that the method described by Cabot and Holland in 1932 is the most desirable. It is emphasized that in utilizing this procedure it is unnecessary to mobilize the kidney to any great extent except on its posterior surface. This technic involves insertion of an instrument, such as a uterine sound roughly curved in the shape of a U, through the pelvis and lower calix to the desired point on the cortical surface of the kidney. A linen suture is then tied around the bulbous end of the sound, which is pulled back through the pelvis. The suture is removed from the sound and secured on the end of a Malécot catheter, which has been previously cut to a taper; it is then pulled by the linen suture through the pelvis of the kidney and out the lower calix so that the tip of the catheter is accurately placed in the renal pelvis. Nephrostomy performed in this manner involves less damage to the renal parenchyma than when it is carried out by older methods which involve the insertion of curved forceps through the parenchyma. The postoperative care involves roentgenographic examination to determine the exact position of the tube in the kidney. This is best done by taking one film without injecting any medium and then taking one after moderately filling the pelvis with the desired opaque solution. The tube should not be removed for at least ten days, and if longer drainage is desired the original tube should be left in position; in general, as long as it drains satisfactorily and does not become encrusted.

Uretero-enterostomy may be indicated for a number of conditions, namely, congenital abnormalities, inoperable vesicovaginal fistula, intolerable vesical tuberculosis, intractable interstitial cystitis and cancer of the bladder. In general, the operation should be confined to those patients whose ureters are within approximately normal limits in size. Careful preoperative preparation of the intestinal tract by use of a low residue diet and cleansing enemas is of great importance. The author stated a preference for a two stage operation, with transplantation of one ureter at a time. The loop of sigmoid colon to be utilized is drawn through an incision in the peritoneum. After the completion of the anastomosis, the intestine is fixed to the peritoneum in such a way that the line of suture is extraperitonealized. The chief contraindication to the two stage operation is cancer of the bladder, in which case bilateral uretero-enterostomy may be desirable as a single operation. The portion of the ureter that is mobilized should be that which leads directly from the brim of the pelvis to the point on the intestine selected for anastomosis.

After uretero-enterostomy, the patient should be given fluids plentifully, either subcutaneously or intravenously. A rectal tube is kept

constantly in place for from ten to fourteen days. Nothing is given by mouth for forty-eight hours, and then small amounts of water are given for the next several days, after which a liquid diet, without milk, is administered for a few more days. Enemas are contraindicated for at least ten days. When the patient's condition permits, the status of the kidneys should be determined by intravenous urography.

Cutaneous ureterostomy is almost exclusively reserved for cases in which the ureters are grossly abnormal. Under such circumstances the ureters are dilated and readily permit the introduction of a fairly large sized, soft rubber catheter. The most desirable point for bringing the ureter to the abdominal wall is just medial to the anterosuperior iliac spine. The ureter is exposed and mobilized through an oblique incision, the center of which lies on a line between the anterosuperior iliac spine and the umbilicus. The ureter is freed down into the pelvis for a distance sufficient to permit the lower end of the ureter to be brought into the wound and project beyond the skin for a distance of several centimeters. The ureter should also be freed well above the pelvic brim in such a way that it can be brought out through the incision in a gentle curve without any kinks. The ureter should be brought through the skin obliquely and not at a right angle, as the latter technic will tend to cause too sharp a bend in the ureter just below the abdominal wall. A soft rubber catheter of a size that fits snugly in the lumen of the ureter is inserted into the renal pelvis, and the satisfactory position of the tube is determined by complete aspiration of all the solution that is injected. The catheter is then held in position by two catgut ligatures which are placed one above the other close to the distal end of the ureter. No sutures are placed through the ureter.

Postoperative care in cases in which cutaneous ureterostomy has been performed involves roentgenographic examination to determine definitely the position of the tube in the renal pelvis. After the protruding portion of the ureter has sloughed off, leaving a pouting roset of mucous membrane on the abdominal wall, the catheter is maintained in position by heavy silk ties attached to pieces of adhesive tape placed at right angles to the wound. The renal pelvis is irrigated daily with a bland solution. Subsequently the necessity of irrigating the kidney depends on the amount of infection and dilatation that is present. There is considerable variation in the frequency with which the catheter should be changed. This may vary from several weeks to several months or more. No dogmatic rule can be made. The catheter should be changed with sufficient frequency to maintain complete and adequate drainage and to avoid encrustation of the catheter.

ANURIA

Cubitt¹⁰³ reported 2 cases of anuria and discussed the problems relating to this condition, particularly the reflex type, as exemplified by the renorenal or ureterorenal reflex when an obstruction on one side is capable of producing suppression in the contralateral kidney which is otherwise normal.

He said that the unobstructed kidney in cases of reflex anuria is enlarged and deeply congested. This refutes the hypothesis of a reflex vascular spasm or cramp, for the contralateral kidneys should then be small, pale and bloodless.

Recent studies on secretion of urine have disclosed that in the normal unobstructed kidney there is a certain intrarenal pressure acting in all directions within the capsules of the organ and tending to obliterate the tubules, thus offering a constant resistance to the production of urine. Increase of this intrarenal pressure through edema, ureteral obstruction with increased intrapelvic pressure or venous obstruction would result in a diminished output of urine.

It is possible that spasm of one ureter in response to impaction of a stone sets up afferent nervous impulses which, either by direct reflex action or by release of some hormone (epinephrine or posterior pituitary), cause vascular changes in the other kidney, an alteration in capillary permeability and an exudation of fluid into the renal parenchyma; the increased intrarenal pressure obstructs the tubules and raises the pressure of urine, opposing filtration; at the same time it causes partial obstruction to the venous outflow, so that the kidney is congested with blood.

In one of Cubitt's cases spinal anesthesia was used in addition to the administration of dextrose solution intravenously and ureteral catheterization, so that it was impossible to attribute the successful result which was obtained to any one type of treatment separately.

However, spinal anesthesia is put forward as a rational therapeutic measure worthy of trial in cases of reflex anuria. This applies whatever the etiology, since the afferent path at least must be a nervous one.

TRICHOMONAS

Allen¹⁰⁴ stated that vaginitis caused by *Trichomonas vaginalis* is one of the common gynecological diseases. High dry magnification of the fresh, unstained vaginal secretion under reduced illumination simplifies

103. Cubitt, A. W.: The Problem of Anuria: A Review of Recent Work on Renal Physiology, with Reports of Two Cases, *Brit. J. Surg.* **24**:215-226 (Oct.) 1936.

104. Allen, Edward: *Trichomonas Vaginalis Vaginitis*, *Am. J. Surg.* **33**: 523-528 (Sept.) 1936.

diagnosis. Later staining of the dried secretion will serve to distinguish the other common forms of vaginal infection, such as yeast infection and gonorrhea.

The profuse bubbly discharge which is found in this condition is also laden with various strains of streptococci. These streptococci may invade the urinary tract, Bartholin's glands and probably the deeper structures of the pelvis. In like manner, the urinary tract of the male may become infected during coitus either by the coccoid organisms or by the motile flagellates themselves, and a troublesome urethritis or prostatitis is the result. Constant reinfection of the female renders permanent cure impossible until the focus in the male has been treated.

Permanent cure of vaginitis caused by *Trichomonas* will depend on recognition of these possible avenues of infection. Elevation of the general resistance of the patient is important in the therapy.

STERILIZATION

Baer¹⁰⁵ stated that sterilization is permissible in any woman in whom pregnancy will aggravate existing disease which is not amenable to direct cure, undo previous corrective gynecological procedures or jeopardize her life. Written consent from both husband and wife should be obtained. Sterilization is urgently desirable in women with certain types of mental disease and congenital defects.

For permanent sterilization by surgical methods, tubal crushing and cornual excision are the simplest and surest of all the available methods. When surgical methods are contraindicated, permanent sterilization can be obtained by either roentgen or radium therapy. This always involves destruction of ovarian function and onset of the menopause.

Temporary sterilization by surgical methods is usually a failure. Irradiation for this purpose is unreliable and fraught with the risk of producing permanent sterilization. Contraception is the logical procedure if pregnancy is to be avoided temporarily.

Combined sterilization and therapeutic abortion are indicated in approximately 13 per cent of cases in which sterilization is necessary. Abdominal hysterotomy by a transverse fundal incision, which includes cornual excision, is the operation of choice.

Biologic methods for the attainment of sterilization are still entirely experimental. The only one that holds any hope in the future is the utilization of spermatotoxins.

Hagner¹⁰⁶ stated that the most frequent cause of sterility in the male is inflammatory occlusion of the epididymis or vas deferens. Atrophy

105. Baer, J. L.: Sterilization, *Am. J. Surg.* **33**:513-517 (Sept.) 1936.

106. Hagner, F. R.: The Operative Treatment of Sterility in the Male, *J. A. M. A.* **107**:1851-1854 (Dec. 5) 1936.

of the testis rarely occurs in epididymitis, especially in the type associated with gonorrhea. Traumatic epididymitis rarely leads to sterility.

Hagner has never had a successful case after operation for sterility in which the patient has not had a history of bilateral epididymitis. There are two conditions that must be present for a successful result in sterility of this type: 1. The vas must be patulous above the point of anastomosis. 2. The globus major, or the upper portion of the body of the epididymis, must contain live spermatozoa. He has had no successful results except in cases in which silver wire was used as a suture. Hagner only briefly mentioned the steps of the operation, as these have been reported many times already and repetition is unnecessary. It is important to control all bleeding either by torsion or by pressure before the anastomosis is made. He has always done a bilateral operation, being careful not to make the incision in the vas too high up, thus giving a double chance for a cure and, in case of failure the first time, allowing for a subsequent operation.

In the 65 cases Hagner reported 77 operations were performed. In 12 cases a second operation was necessary because of initial failure. Of these 12 patients, 7 were cured by the second operation. Nearly all the operations were done by lateral anastomosis except the few rather atypical ones already mentioned. Sometimes one finds occlusion of the vas at the first incision, and by going further up the vas one is able to get above this obstruction. Unless great care is exercised to cut only into the lumen of the vas, which is recognizable by the yellowish tinge of its lining, there is likelihood of the operator carrying the incision through the entire diameter of the tube. It is important not to strip the vas deferens too close. Hagner places the first suture at the distal end of the incision in the vas, taking a good heavy bite, as this is the anchoring suture for the operation and the obstruction is below this point. The suture is then anchored firmly in the lower end of the elliptic incision of the epididymis. Two lateral sutures are then placed to take a fairly heavy bite in the epididymis and include some of the cut tubules. If only the fibrous covering of the epididymis is taken up in the suture, the cut tubules drop back when the anastomosis is made. The suture is then passed through the cut edges of the vas, just enough tissue being taken to approximate the edges. The last suture is passed in the same way through the upper end of the incision in the epididymis. It is then passed through the vas, at the upper angle of the incision, being carefully placed so as not to occlude the lumen. Hagner tests this out with a tear duct probe. The anastomosis is then complete. The instruments that he uses are iridectomy knives, scissors and artery forceps, such as those commonly used in operations on the eye.

Hagner stated that the operation, while tedious, is not dangerous to life. He always uses general anesthesia. He stated that in order to avoid the formation of scar tissue local infiltration should not be used. The operation cannot compromise the function of an organ that has already proved functionless. In no class of cures will the surgeon be rewarded by his patients with a greater warmth of gratitude.

REJUVENATION

Blum,¹⁰⁷ after discussion of the philosophic and physiologic aspects of old age and rejuvenation, took up the different types of operations and treatments for rejuvenation that have been put forth in the last years, since the first publication of Steinach in 1920. These included Steinach's operations and modifications, sympathicodiaphtheresis, transplantation of sexual glands and nonoperative treatment, such as diathermy, roentgen therapy, hormonal therapy and psychotherapy. Blum confined his paper to rejuvenation in the male.

Steinach's theory can be reviewed briefly as follows: The testis is composed of two parts, the spermatogenic and the hormonal. Old age is attributable to atrophy of the hormonal part of the testis. By ligation of the vas deferens, sperms are kept back, the spermatogenic epithelial cells atrophy by pressure, and the interstitial cells, the carriers of the hormonal production, hypertrophy.

Blum has used vasoligation in many hundred cases, mostly in patients suffering from prostatic obstruction. He has never been able to find any lasting rejuvenating effect that could not be attributed to other causes (relief of symptoms by relief of prostatic obstruction, etc.). Extensive experiments on animals (Romeis, 1933) never demonstrated any hypertrophy of the interstitial cells after vasoligation, so that Steinach's theory lacks real proof. The same is true for all modifications of Steinach's first described operation.

Not much better founded is Doppler's operation, which consists in a chemical sympathectomy of the blood vessels to the testis. By that means the blood flow to the testis is increased, but the effect wears off much too soon. Better results are obtainable from the transplantation of testes and, without any operation, from the injection of hormonal substances, especially androgen. The underlying thought in all treatments for rejuvenation, or as Blum would prefer to call it, reactivation and regeneration, is an increased circulation of hormones in the organism. It is essential that the hormones find an organism which is still able and ready to react to them. This increase of hormones can

107. Blum, Viktor: *Verjüngung und Verjüngungsoperationen*, Wien. med. Wchnschr. 86:989-994 (Sept. 5) 1936.

be reached by injection or by activation of endocrine glands by treatment with diathermy, roentgen rays and ultraviolet light. Those measures should be tried out first, and operation, with its short effect, performed only in exceptional cases.

UROGRAPHY

Osterberg¹⁰⁸ was prompted to describe the opaque medium used by the Section on Urology at the Mayo Clinic for the purpose of retrograde pyelography because of frequent inquiry as to its composition and preparation. This medium has been used for several years and has been satisfactory.

It is prepared as follows:

Hippuran crystals, 160 Gm., are dissolved in 200 cc. of commercially prepared solution which contains metaphen, 1:2,500. This quantity is increased to 800 cc. by the addition of a solution of 6 per cent acacia and 1 per cent sodium chloride. This 6 per cent solution of acacia is the same as that used for intravenous purposes. Addition of acacia results in precipitation of a small amount of hippuran. This precipitate is filtered off on a Buchner funnel, and the clear solution is placed in 15 cc. cotton-stoppered tubes. These are autoclaved, and the medium is ready for use. If difficulty is encountered in obtaining a clear solution, filtration through a pad of infusorial earth may be resorted to. The resulting solution contains approximately 20 per cent hippuran, 4 per cent acacia and metaphen, 1:10,000, to insure self-sterilization.

108. Osterberg, A. E.: Preparation of Medium for Retrograde Pyelography. Proc. Staff Meet., Mayo Clin. **11**:560 (Aug. 26) 1936.

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INTERNAL FIXATION OF FRACTURES OF THE NECK OF THE FEMUR

MELVIN S. HENDERSON, M.D.

ROCHESTER, MINN.

A fracture of the neck of the femur is a serious injury and to the aged person it is practically a death blow. Because of the teachings of two midwestern surgeons, Ruth and Maxwell, and as a result of the work of Royal Whitman, the medical profession a generation ago became aware that union could be obtained after this type of fracture in a fair proportion of cases if rational and efficient treatment was promptly instituted. Sufficient data have now been gathered to enable one to evaluate Royal Whitman's method,¹ which is almost universally used in America. A commission appointed by the American Orthopaedic Association² reported that bony union was secured by the Whitman method in about 50 per cent of the cases in which the patients were less than 60 years of age, but that in cases in which the patients were more than 60 there was a sharp decrease in the percentage of good results. The mortality incident to the accident and treatment varied, but the average was about 15 per cent. Furthermore, the report definitely indicated that results were better where some form of internal fixation was provided.

The reasons for such unsatisfactory results following conservative measures are many. It is not sufficient to blame the advanced age of the patient, because other fractures in an elderly person unite readily.

ANATOMIC STRUCTURE

The crux of the situation rests in the anatomic structure of the neck and head of the femur. The proximal fragment cannot be controlled because there is no way of grasping it, so the lower fragment must be brought into alinement and maintained there. If the fragments

From the Section on Orthopedic Surgery, the Mayo Clinic.

1. Whitman, Royal: The Abduction Method, Considered as the Exponent of a Treatment for All Forms of Fracture at the Hip in Accord with Surgical Principles, *Am. J. Surg.* **21**:335-344 (Sept.) 1933.

2. Report of a Commission Appointed by the American Orthopaedic Association to Study the End Results of Intracapsular Fractures of the Neck of the Femur, *J. Bone & Joint Surg.* **12**:966-969 (Oct.) 1930.

are not securely held in this position, the shearing force that is produced by the pull of the powerful pelvic and femoral muscles and by the angle that the neck of the femur forms with the shaft, which is about 127 degrees, will either cause angulation at the site of fracture or cause the lower fragment to slip upward. The capsule of the hip joint may be so torn that it will lie between the fragments. This is probably a rare happening, but I have found it when the joint was opened in several cases. Gaenslen³ recently reported a series of experiments in which fractures of the hips of dogs were produced by arthrotomy. Although the capsule was tucked in and held by sutures between the fragments, bony union was secured if the fragments were spiked together with knitting needles. His only failure to obtain union was in an animal in which he used Kirschner's wires instead of the more rigid knitting needles to provide fixation. The wires failed to maintain fixation, and Gaenslen⁴ concluded that the failure to maintain fixation led to nonunion.

BLOOD SUPPLY

The blood supply may be interfered with by the trauma incident to the accident. The blood supply of the head and neck of the femur is derived from four sources: the diaphysis, the epiphysis, the ligamentum teres femoris and the periosteum. The vessels which come from the diaphysis cross the epiphysial line to enter the head of the femur. The epiphysial blood vessels enter the head of the femur, along the edge of the articular surface, close to the epiphysial junction. Two groups of epiphysial vessels are recognized: One group comes from the subtrochanteric fossa and enters the head of the femur from above; the other group comes from the region about the insertion of the articular capsule on the inferior aspect of the neck of the femur and enters the lower end of the head of the bone. Blood vessels are carried by the ligamentum teres femoris. It is probable that the blood supply derived from the ligamentum teres femoris is so meager as to be of no value in about 25 per cent of elderly persons.⁵ In the new-born a free blood supply through this ligament is always present. Kolodny⁶ expressed the belief that the periosteal group of vessels were important, and he satisfied himself that the portion of the neck of the femur lying within

3. Gaenslen, F. J.: Fracture of the Neck of the Femur, *J. A. M. A.* **107**: 105-114 (July 11) 1936.

4. Gaenslen, F. J.: Subcutaneous Spike Fixation of Fresh Fractures of the Neck of the Femur, *J. Bone & Joint Surg.* **17**:739-748 (July) 1935.

5. Wolcott, W. E.: Circulation of the Head and Neck of the Femur: Its Relation to Nonunion in Fractures of the Femoral Neck, *J. A. M. A.* **100**:27-33 (Jan. 7) 1933.

6. Kolodny, Anatole: The Architecture and the Blood Supply of the Head and Neck of the Femur and Their Importance in the Pathology of Fractures of the Neck, *J. Bone & Joint Surg.* **7**:575-597 (July) 1925.

the capsule possessed a periosteum which differed little, if at all, from the periosteum of the extracapsular portion of the neck of the bone. Kolodny stated that the diaphysial, periosteal and epiphysial blood vessels were the important ones in the nutrition of the head and neck of the femur of an elderly person. Therefore, it would seem that sufficient blood is supplied to the fractured bone to ensure bony repair if proper apposition of the fragments is maintained.

REDUCTION AND FIXATION

The surgeon, and particularly the inexperienced one, may have difficulty not only in reducing a fracture of the neck of the femur but in providing fixation after reduction. Manipulative reduction should always be checked by roentgenograms, which should be made in the lateral as well as in the anteroposterior position, if possible. Proper reduction and fixation are the essential factors, and failure to provide the latter has led to many poor results.

ASEPTIC NECROSIS

Aseptic necrosis frequently is blamed for the failure of the fracture to unite. Gaenslen, in advocating internal fixation in the treatment of this type of fracture, said that the cause of aseptic necrosis, which too commonly is encountered in unimpacted fractures, is mobility at the site of the fracture. Absolute immobility in any cast is impossible of attainment, and if there is any great amount of absorption at the line of fracture one can readily understand how displacement of the fragments would occur.

SELECTION OF PATIENTS

Unfortunately, every patient who has a fracture of the neck of the femur cannot endure the necessary treatment. The debilitated elderly person who perhaps is suffering from the terminal stage of a constitutional disease may not be a fit subject for the ordeal, and the extremely old and feeble person who is not suffering from any well defined constitutional disability is maintaining himself on such a narrow margin that, as stated before, the accident is nearly always his death blow. The prolonged fixation in a cast incident to the Whitman method has militated more than any other factor against the carrying out of rational treatment. If the wearing of a cast for such a long period could be avoided, or if the time could be materially shortened, any patient who has enough reserve to tolerate a major surgical procedure would be able to withstand the treatment of a fracture of the neck of the femur.

OPERATIVE TREATMENT

In the hope of shortening the period of confinement and inactivity, operative fixation has been advanced at various times, only to be abandoned because no systematic study was made of the end-results in cases

in which the method was used. The poor results of a method in its developmental stage are always viewed with critical eyes and may overwhelm a sound rational procedure, which, if persistently advanced and improved, would hold its place in the surgical armamentarium. Bad news travels as fast in the surgical world as it does in other walks of life.

The Smith-Petersen Nail.—Smith-Petersen,⁷ of Boston, in 1931 reported the use of a triple flanged metal nail in the treatment of fractures of the neck of the femur. The results with this method were so good that attention was promptly attracted to it. Johansson,⁸ of Sweden, and King,⁹ of Australia, have advocated the use of the Smith-Petersen flanged nail, but they use a cannulated nail so that it can be driven in over a guiding wire. The literature on the subject is increasing. Thomas,¹⁰ Knowles,¹¹ Gaenslen,⁴ Moore,¹² Wescott,¹³ W. Meyer¹⁴ and others, including myself, have reported fractures of the neck of the femur which have been treated by internal fixation and have described the technic of the method. Sufficient data have now been recorded to prove that the results with this method are quite good.

Impacted Fractures.—Too often, the surgeon has been lulled into a false sense of security in the treatment of a fracture of the neck of the femur, because the roentgenogram has dissolved what is termed "impaction" of the fragments. The impaction too frequently breaks down and, except in a rare instance, should not be trusted. The rare instance I refer to is the case in which the fracture is situated close to, or involves, the head of the femur; there is really a compression

7. Smith-Petersen, M. N.; Cave, E. F., and Vangorder, G. W.: Intracapsular Fractures of the Neck of the Femur: Treatment of Internal Fixation, *Arch. Surg.* **23**:715-759 (Nov.) 1931.

8. Johansson, Sven: On Operative Treatment of Medial Fractures of the Neck of the Femur, *Acta orthop. Scandinav.* **3**:362-392, 1932.

9. King, Thomas: Recent Intracapsular Fractures of the Neck of the Femur: A Critical Consideration of Their Treatment and a Description of a New Technique, *M. J. Australia* **1**:5-15 (Jan. 6) 1934.

10. Thomas, T. T.: Fixation by a Wood Screw Without Arthrotomy in Certain Fractures of the Neck of the Femur, *Am. J. Surg.* **35**:292-295 (Sept.) 1921.

11. Knowles, F. L.: Fractures of the Neck of the Femur, *Wisconsin M. J.* **35**:106-108 (Feb.) 1936.

12. Moore, A. T.: Fracture of the Hip Joint (Intracapsular): A New Method of Skeletal Fixation, *J. South Carolina M. A.* **30**:199-205 (Oct.) 1934.

13. Wescott, H. H.: Preliminary Report of a Method of Internal Fixation of Transcervical Fractures of the Neck of the Femur in the Aged, *Virginia M. Monthly* **59**:197-204 (July) 1932; A Method for the Internal Fixation of Transcervical Fractures of the Femur, *J. Bone & Joint Surg.* **16**:372-378 (April) 1934.

14. Meyer, W.: Result of Nailing the Head to the Neck in Intracapsular Fracture of the Left Femur, with Excellent Functional Result, *Tr. New York Acad. Med.* **10**:672, 1893.

fracture of the head and the upper portion of the neck of the femur (fig. 1a). An impacted fracture through the middle of the neck of the femur (fig. 1b) or near the greater trochanter should practically always be broken up with the patient anesthetized and the fracture reduced by manipulation. Adequate fixation must then be provided in a plaster of paris cast or by aid of some form of internal fixation.

Methods of Internal Fixation.—Smith-Petersen advised open reduction of the fracture and insertion of the nail by visual supervision. Reduction of the fracture by arthrotomy is truly a major operative procedure and one that should be undertaken only by experienced surgeons. With the so-called "blind" method, the fracture is reduced by

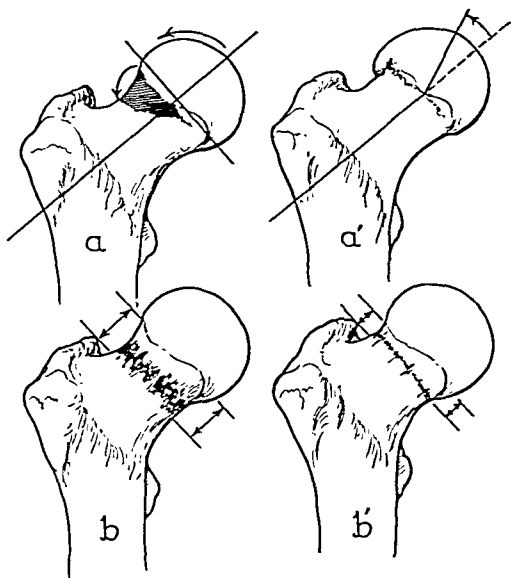


Fig. 1.—In *a* is shown a fracture of the neck of the femur, the darkened area indicating the region of compression; *a'* the position after compression; in *b*, a typical transverse fracture of the neck of the femur, the darkened area showing the region of absorption, and in *b'* union with shortening of the neck of the bone.

one of the recognized manipulative procedures, and after roentgenographic or fluoroscopic examination reveals that reduction has been secured a small incision is made over the greater trochanter and the nail driven through the neck and well into the head of the femur. The "blind" method can be made more accurate by inserting a guiding wire after the apposition of the fragments is known to be accurate and by checking the position of the wire by anteroposterior and lateral roentgenograms. If the position of the wire is satisfactory as to direction and depth, a cannulated flanged nail is passed over it and driven through the neck and into the head of the femur. The wire is then withdrawn.

Insertion of the nail in this manner is not as certain to be accurate as one might expect, because even when the nail is guided by the wire it may wander and bend the wire, particularly as it enters the head of the femur. If the wire is bent to any degree, the end may break off when the wire is withdrawn through the cannulated nail. To prevent this the wire should be passed completely through the head of the femur and should extend into the acetabulum. This steadies the head of the femur as the nail crosses the line of fracture and is driven into the head of the bone. The insertion of the wire and the roentgenographic control of the position is often a prolonged procedure, for the roentgenograms have to be developed. The operation is remarkably safe if done with the patient under spinal anesthesia, for there is practically no dissection or exposure of tissue and so, no shock. I have had no experience with the reduction of such fractures under fluoroscopic control.

Objectionable Features of the Nail.—The flanged nail of Smith-Petersen is strong and in theory, at least, would seem to solve the problem of the treatment of this type of fracture. It at first was hoped it would not be necessary to apply a cast and that weight bearing could be permitted very early, but weight bearing, if permitted before bony union is well under way, has proved disastrous. It is advisable for the patient to wear a cast for from two to six weeks and permit no weight bearing for at least three months. The triple flanged nail of Smith-Petersen has a large area of metal which comes in contact with the bone, and in some instances it is poorly tolerated. Although the nail may have been driven in securely and may have been in excellent position, it may become loose as a result of absorption of bone about it and back out, as it were. How to prevent this is a problem as yet unsolved. Absorption at the line of fracture also occurs in some cases, and as the neck of the femur becomes shorter, the nail, which is firmly embedded in the head of the bone, protrudes beyond the trochanter and becomes loose.

Fixation with a Lag Screw.—Because of this difficulty, at the Mayo Clinic the use of what is called a "lag" screw has been resorted to. This will hold the fragments together. I claim nothing original for the use of the lag screw, as carpenters have long used it in cabinet work when they desired to coapt pieces of wood and it was undesirable to insert a bolt. I do not believe that it has been used previously in just this manner for the fixation of fractures of the hip, though M. O. Henry described a screw bolt similar in principle. It has been used in four cases at the clinic; in one of these cases the fracture was old, and in the others the fractures were recent. Successful results were obtained in three cases; in one case the time which has elapsed since the operation has not been sufficient to permit one to determine the end-result. The

threads in the portion of the screw that goes into the head of the femur are of the wood-screw type; large and little notches are placed along the thread so that it will hold better (fig. 2). The lag screw which has been used at the clinic is cannulated and is inserted over a guiding wire.

DATA IN SIXTEEN CASES IN WHICH INTERNAL FIXATION WAS EMPLOYED

Sex and Age.—Of a group of sixteen patients with fracture of the neck of the femur who were treated with internal fixation, four were men and twelve were women. The distribution of these patients according to the various age groups follows: between 20 and 29 years,

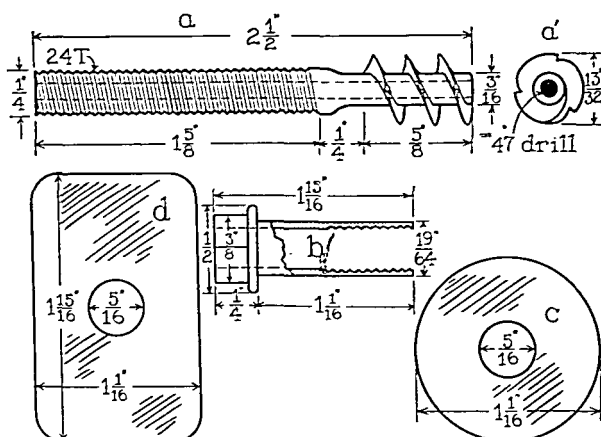


Fig. 2.—Diagram of a lag screw: *a*, the lag screw; *b*, the sleeve nut; *d* and *c* washers, and *a'*, the end view, showing cannulate opening.

one; between 40 and 49 years, one; between 50 and 59 years, four; between 60 and 69 years, five; between 70 and 79 years, four, and between 80 and 89 years, one. Thus, ten of the patients were more than 60 years of age.

Selection of Patients for Operation.—Any patient who was thought fit to withstand a major surgical operation was subjected to the procedure. The majority of patients were operated on as soon as the general examination was completed, and all were subjected to operation within three weeks of the accident. King, of Melbourne, Australia, prefers to make the patient comfortable and to wait three weeks before operating. By the end of that time he has a good idea as to the fitness of the patient for operation.

Anesthesia.—Spinal anesthesia is preferable; this type of anesthesia was used in eleven of the sixteen cases.

Type of Operation.—Arthrotomy was done in three cases. This permits visual supervision of the reduction of the fracture and the insertion of the nail. In the remaining thirteen cases closed reduction was done by Leadbetter's¹⁵ method, and the nail or screw was inserted along a Kirschner wire, which was used as a guide. A cannulated Smith-Petersen nail was used in thirteen cases, a cannulated plain screw with a large thread in one case and the cannulated lag screw in two cases. The roentgenographic examination at the time of reduction showed perfect and complete reduction in nine cases. In seven cases there was overcorrection of the deformity; that is, the head of the femur was in a valgus position, which really is a desirable position, for I cannot recall

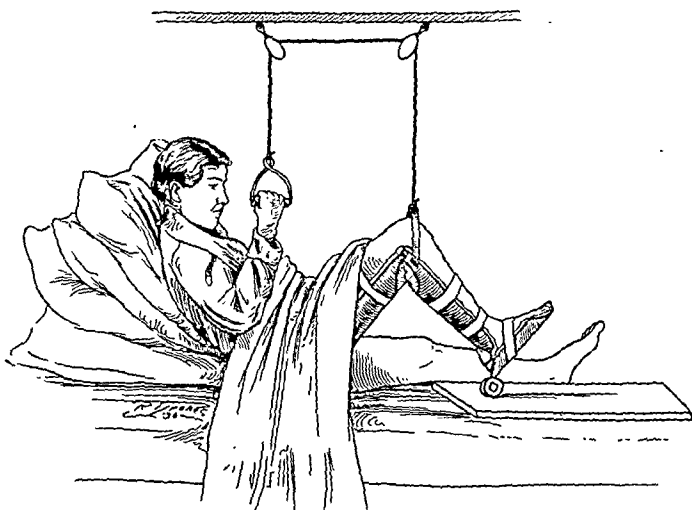


Fig. 3.—Apparatus for moving the hip.

that I ever have seen such a fracture overcorrected in this manner fail to unite. Preoperative classification of the fractures disclosed that one was oblique, five were transverse, and nine were impacted. All the fractures were in the neck of the femur; no trochanteric fractures are included in this series.

External Fixation and Institution of Motion.—In treatment of these patients at the clinic either a single spica cast, which extended downward to the knee or a double spica, which extended from the thorax to the toes on the affected side and to the knee on the sound side, was used. The cast was bivalved or was removed in two weeks so as to permit bending of the knee, unless there was some complicating factor. Motion was instituted by aid of a sling placed under the knee, and this was

15. Leadbetter, G. W.: A Treatment for Fracture of the Neck of the Femur. *J. Bone & Joint Surg.* 15:931-940 (Oct.) 1933.

pulled by the patient by means of a rope which passed through a pulley on an overhead bar (fig. 3). By this contrivance the hip is moved as the patient moves the knee.

Weight Bearing.—The patients, on the average, were allowed up on crutches in seven weeks, and partial weight bearing was permitted. Full weight bearing without support of any kind was permitted, on the average, in four and a half months (fig. 4A).

Days Spent in Hospital.—The number of days spent in the hospital averaged sixty-eight.

Removal of the Nail.—When union is complete the nail had better be removed (fig. 4B). However, one patient who was past 80 years



Fig. 4.—A, fracture of the hip united three and a half months after insertion of a lag screw. B, union of the fracture of the hip shown in A. The roentgenogram was made after removal of the lag screw.

of age lived comfortably for two years with good function in spite of the fact that the nail was never removed.

RESULTS

There was no postoperative death or serious infection, although low grade infection developed late in two cases. Solid bony union has been secured in thirteen of the sixteen cases; one fracture definitely has failed to unite, and in two cases the results are as yet indeterminate. Therefore, of fourteen cases in which sufficient time has elapsed to be

certain of the result, in thirteen, or 92.8 per cent, bony union has been obtained. In the six cases in which the patient was less than 60, the fractures united solidly. In two of the ten cases in which the patient was more than 60, the results are still indeterminate; that is, bony union is not demonstrable in the roentgenogram. I feel confident that one of these fractures will unite, but I am not so certain about the other one. In one case the result may be classified definitely as a failure. Bony union therefore occurred in seven, or 87.5 per cent, of the eight cases in which the convalescence had progressed far enough to enable one to determine the end-result.

Results of Internal Fixation in Sixteen Cases of Fracture of Neck of Femur

1. Entire group of cases.....	16
Deaths following operation.....	0
Low grade infections (late).....	2
Patients still under observation.....	2
Cases in which nonunion occurred.....	1
Cases in which bony union occurred.....	13*
2. Patients less than 60.....	6
Cases in which bony union occurred.....	6
3. Patients more than 60.....	10
Cases in which nonunion occurred.....	1
Patients still under observation.....	2
Cases in which bony union occurred.....	7†

* This number represents 92.8 per cent of the fourteen cases in which end-results could be determined.

† This number represents 87.5 per cent of the eight cases (group 3) in which the end-results could be determined.

COMMENT

The reason for the decided interest shown in the internal fixation of fractures of the neck of the femur is that the results following the conservative treatment were on the whole unsatisfactory.

The results obtained in this limited number of cases at the clinic are far better than were ever obtained there in a similar group of cases in which the fractures were treated conservatively. The sharp pains that occur commonly after conservative reduction are absent in cases in which the fracture is treated by internal fixation, because the fixation is absolute. Many of the patients do not have the slightest pain. Furthermore, when internal fixation is employed the patient is much more comfortable during convalescence. The discomfort that the patient endures when he tries to limber up after he has spent three months in a cast is not encountered because early mobility of knee and hip is possible when internal fixation is employed. The effect on the morale of the patient is an exceedingly happy one. There were no deaths in the

series of cases in which this type of treatment was employed at the clinic. I believe the danger of pulmonary embolism is decreased because the patients can be moved about early, active motion is permitted and the blood is kept circulating in the iliac vessels.

Pitted against these favorable aspects are an array of objections which must be considered. The insertion of the Smith-Petersen nail, the lag screw, pins or a bone graft is not easy, and the surgeon too often is chagrined and startled to find how far wrong his aim was in the insertion of these objects. This has been acknowledged by all and has led to the manufacture of many gadgets and instruments designed to overcome this difficulty. The specter of infection always hovers about these procedures. An infected hip means either death or prolonged drainage with all its discomforts, and experience with such a condition is sufficient to dampen the ardor of even the most enthusiastic surgeon. This type of operation must be done only in a properly equipped hospital and by an experienced surgeon. The nail does not always stay where it is put, for absorption about the nail may cause it to become loose and slide outward. Absorption of the neck of the femur at the site of fracture may so shorten the neck of the bone that even if the end of the nail stays in the head of the femur the head of the nail may protrude considerably beyond the trochanter and the action of the muscles during movement may further tend to loosen it. It takes at least three months for bony union to occur, and even with perfect internal fixation, full weight bearing cannot be permitted until roentgenographic examination discloses that bony union is present. While it is true that a larger percentage of patients with fractures of the neck of the femur can be treated by this method than by the Whitman method, because prolonged wearing of a cast is not necessary, if internal fixation is used indiscriminately in all cases of fracture of the neck of the femur, failures and disasters will follow and will tend to discredit the method. The incidence of fractures of the hip compared to other fractures is relatively small, so that the experience of any one man is meager unless he is in a surgical center and by agreement the patients are referred to him; therefore, the operative treatment of these fractures should be centralized and experience provided. Time will disclose whether flattening and distortion of the head of the femur are less frequent following the use of internal fixation than they are following the use of the closed method.

SUMMARY

I believe that internal fixation of fractures of the neck of the femur gives better results with no higher mortality than does conservative

treatment. Therefore, internal fixation should be employed when it can be carried out in the proper surroundings and by a surgeon of sufficient training in surgical operations on the bones. Lacking such conditions, it is better either to refer the patient to a hospital where the exacting conditions can be fulfilled or to treat the patient by such conservative methods as the surgeon is familiar with. There is no hurry in carrying out internal fixation. One authority, King, of Australia, prefers to wait three weeks and thus escape the high early mortality that is encountered in conjunction with this serious injury.

- CARCINOMA OF THE GALLBLADDER

WILLIAM A. COOPER, M.D.

NEW YORK

Carcinoma of the gallbladder, a rare condition in 1850, has since become a common one. The apparent increase in the incidence of the disease roughly parallels the increase in the frequency of operations on the gallbladder. The purpose of this paper is to add to the literature the data on 48 cases of carcinoma of the gallbladder observed at the New York Hospital from 1915 to 1935. After a brief historical review, the cases are analyzed pathologically, the pathogenesis being emphasized whenever possible. The same cases are then considered clinically in an attempt to clarify the clinical picture and thereby to aid in early diagnosis.

HISTORICAL REVIEW

In 1777 Maximilian Stoll,¹ of Vienna, published the first authentic record of carcinoma of the gallbladder, reporting 2 cases in which autopsy was performed. His first case not only introduced a new group of diseases but was unique, the patient having situs inversus viscerum, with carcinoma of the left-sided gallbladder. Hallé² in 1786 reported the next case, followed by Baillie's³ case in 1794, the authenticity of which has been questioned.

From 1800 to 1850 but 9 cases were reported, in 2 of which the lesions probably were secondary. The first full account appeared in this period—the case of Durand-Fardel⁴ in 1838.

From 1850 to 1860 9 more cases were recorded. Heschl⁵ in 1852 reported 1 case and referred to 2 others which he had observed, both of which were associated with cholelithiasis.

From the Department of Surgery of the New York Hospital and Cornell Medical College.

The Department of Pathology of the New York Hospital furnished the autopsy material herein presented.

1. Stoll, Maximilian: *Rations medendi*, in *Nosocomio practico Vindobonensi*, Vienna, A. Bernardi, 1777, pt. 1, p. 290.

2. Hallé, Jean Noël: *Histoire de la société de médecine*, 1786 (Paris, 1790), p. 125.

3. Baillie, M.: *Anatomie des krankhaften Baues von einigen der wichtigsten Theile im menschlichen Körper*. Aus dem Englischen mit zusätzen von S. T. Sömmering, Berlin, Leopold Voss, 1794.

4. Durand-Fardel, C. L.: *Note pour servir à l'histoire des maladies de la vésicule biliaire*, *Bull. Soc. anat. de Paris* **13**:157-160, 1838.

5. Heschl, R.: *Ein Fall von Zottenkrebs der Gallenblase*, *Ztschr. d. k.-k. Gesellsch. d. Aerzte zu Wien* **2**:251, 1852.

The decade from 1860 to 1870 enriched the literature by 15 cases. In 1870 Villard⁶ collected reports of 26 cases, contributing the most complete study up to that time. Musser⁷ in 1889 analyzed 100 cases; Courvoisier⁸ in 1890 devoted a chapter in his "Pathologie und Chirurgie der Gallenwege" to a summary of 103 cases; Ames⁹ in 1894 published his treatise, and carcinoma of the gallbladder, though uncommon, ceased to be rare.

Whereas nineteenth century writers acquainted one with the clinical and the pathologic picture of the disease, it remained for authors of the present century to emphasize its frequency. Notable contributors to the subject since 1900 are Sherrill,¹⁰ Robson,¹¹ Moynihan,¹² Cotte,¹³ Mayo,¹⁴ Quenu,¹⁵ Rolleston,¹⁶ Smithies,¹⁷ Fawcett and Rippmann,¹⁸ Deaver,¹⁹ Lentze²⁰ and recently Illingworth.²¹ It is estimated that at least 2,000 cases have now been reported in the literature.

6. Villard, Ferdinand: *Etude sur le cancer primitif des voies biliares*, Bull. Soc. anat. de Paris **44**:217, 1869; Paris, A. Delahaye, 1870.

7. Musser, J. H.: *Primary Carcinoma of the Gallbladder and Bile Ducts*, Boston M. & S. J. **121**:525-529, 1889.

8. Courvoisier, L. G.: *Casuistisch-statistische Beiträge zur Pathologie und Chirurgie der Gallenwege*, Leipzig, F. C. W. Vogel, 1890.

9. Ames, D.: *Primary Carcinoma of the Gall-Bladder*, Bull. Johns Hopkins Hosp. **5**:74-80, 1894.

10. Sherrill, J. G.: *Cancer of the Gall-Bladder and Ducts*, Ann. Surg. **44**:866-892, 1906.

11. Robson, A. W. M.: *Adenoma of the Gall-Bladder*, Med.-Chir. Tr., London **88**:229-231, 1905.

12. Moynihan, B. G. A.: *Gall-Stones and Cancer*, Lancet **1**:1227, 1905.

13. Cotte, G.: *Traitement chirurgicale du cancer des voies biliares*, Rev. de chir. **39**:1135-1152, 1909.

14. Mayo, W. S.: *Carcinoma of the Gall-Bladder and Bile Passages*, in *Collected Papers by the Staff of St. Mary's Hospital, Mayo Clinic, Philadelphia*, W. B. Saunders Company, 1910, vol. 2, pp. 144-150.

15. Quenu, L.: *Cancer des conduits biliares*, Rev. de chir. **39**:245-266, 1909.

16. Rolleston, H. D., and McNee, J. W.: *Diseases of the Liver, Gall-Bladder, and Bile-Ducts*, ed. 3, New York, The Macmillan Company, 1929.

17. Smithies, F.: *Primary Carcinoma of the Gall-Bladder: An Analysis of Twenty-Three Proved Cases*, Am. J. M. Sc. **157**:67-74, 1919.

18. Fawcett, J., and Rippmann, C. H.: *Carcinoma of the Gall-Bladder Associated with Gall-Stones*, Guy's Hosp. Rep. **67**:41-80, 1913.

19. Deaver, J. B.: *Carcinoma of the Gall-Bladder*, M. Rec. **96**:47-49, 1919.

20. Lentze, F. A.: *Gallensteine und Gallenblasenkarzinom*, Beitr. z. klin. Chir. **137**:38-62, 1926.

21. Illingworth, C. F. W.: *Carcinoma of the Gallbladder*, Brit. J. Surg. **23**:4-18, 1935.

INCIDENCE

This glimpse of the history of the disease fails to convey a concept of the frequency of carcinoma of the gallbladder. It probably is impossible, in the absence of compulsory necropsies, to relate its true incidence. The most reliable sources of information are large series of autopsies.

To estimate the frequency of the disease on the basis of cases in which operation was performed gives a distorted view, for these are selected. This fact may contribute to the general difference in attitude between the surgeon and the internist toward disease of the gallbladder. It certainly represents the origin of widely differing opinion concerning the frequency of carcinoma of the gallbladder. Table 1 shows the incidence of the disease in several large series of operations and autopsies. The surgical incidence, it will be noted, is more variable

TABLE 1.—*Incidence of Carcinoma of the Gallbladder at Operation and Autopsy*

Author	Operations on Gall- bladder	Autop- sies	Carcinoma of Gall- bladder	Incidence, Percentage
Erdmann: New York M. J. 111 : 705-707, 1920.....	224	15	6.70
Illingworth ²¹	1,657	34	3.20
Smithies ¹⁷	1,000	23	2.30
Deaver ¹⁹	1,000	16	1.60
Judd and Gray: Surg. Gynee. & Obst. 55 : 305-315, 1932..	22,365	212	1.00
Illingworth ²¹	8,490	36	0.42
Fawcett and Rippmann ¹⁸	592	48	0.81
von Berenscy and von Wolff: Ztschr. f. Krebsforsch. 21 : 109-118, 1924	19,908	300	1.50

and several times greater than the autopsy incidence in the experience of many authors.

The data in the 48 cases of the New York Hospital were compiled from surgical and autopsy material. Forty-five cases were found in a group of 1,500 operations on the gallbladder, a surgical incidence of 3 per cent. The remaining cases were not discovered at operation. Of the 2,941 autopsies performed between 1915 and 1935, 18 showed carcinoma of the gallbladder, an autopsy incidence of 0.61 per cent.

AGE AND SEX DISTRIBUTION

The age incidence of carcinoma of the gallbladder closely corresponds to that of cancer as a whole. Most cases occur in persons between the ages of 50 and 60. It is interesting to note that inflammatory disease of the gallbladder is most common in persons between 40 and 50, some ten years earlier.

The youngest patient on record is a 22 year old boy (Proescher ²²). Several cases are recorded in persons in the third decade. The oldest patient was mentioned by Illingworth ²¹ as being 95.

22. Proescher, F.: A Remarkable Case of Carcinoma of the Gallbladder in a Man Twenty-Two Years Old, J. A. M. A. 48:481-483 (Feb. 9) 1907.

The age distribution in several groups of cases is shown in table 2. The average age in this series is 53.6 years; the youngest patient was 28 and the oldest 85.

Carcinoma of the gallbladder is more common in women than in men, the ratio being roughly 4:1. The proportion probably is due to the preponderance of cholelithiasis in women. In most series from 80 to 90 per cent of the patients are women. In this group 77 per cent were women.

ETIOLOGY

Probably there is no truer concept of the etiology of carcinoma of the gallbladder than of cancer of any other organ. Cohnheim's theory of embryonic rests has been invoked, especially to explain squamous carcinoma of the gallbladder. Some English authors have thought heredity significant. Multiple papillomas of the gallbladder have been

TABLE 2.—*Age Distribution in Several Groups of Cases*

Years	All Cancer,* Percentage	Judd and Gray's,† Percentage	Author's Series Percentage
1-9.....	0.5
10-19.....	0.5
20-29.....	1.3	0.9	2.0
30-39.....	4.6	4.5	4.2
40-49.....	12.6	14.9	25.4
50-59.....	21.7	40.3	31.2
60-69.....	27.1	33.1	20.8
70-79.....	23.1	6.0	4.2
80-89.....	7.5	2.0
90-99.....	0.6

* United States Mortality Statistics, 1932, pp. 134-135.

† Surg., Gynec. & Obst. 55: 308-315, 1932.

considered precancerous. The mass of evidence on the incidence of cholelithiasis in cancer of the gallbladder established chronic irritation as a more likely predicant. Experimental studies, while inconclusive, support this theory.

Relation of Cholelithiasis.—In Musser's cases of carcinoma of the gallbladder the incidence of cholelithiasis was 69 per cent; Janowski's²³ series represented the other extreme, with an incidence of 100 per cent. In the 890 cases reviewed by Lentze²⁰ in 1926, the incidence of cholelithiasis was 83 per cent. In the remaining 17 per cent, carcinoma was superimposed on inflammatory lesions. In the present series the incidence of cholelithiasis was 79 per cent. Lancereaux²⁴ and others expressed the belief that stones are formed secondary to carcinoma. The weight of evidence is contrary to this view. In 48 per cent of the cases at the New York Hospital there was a history of colic of long duration.

23. Janowski, W.: Ueber Veränderungen in der Gallenblase beim Vorhandensein von Gallensteinen, Beitr. z. path. Anat. u. z. allg. Path. 10:449-480, 1891.

24. Lancereaux, M.: Du cancer de la vésicule biliaire, Semaine méd. 7:334. 1887.

and many of the stones were of the calcified type, which are known to form slowly. Furthermore, Graham²⁵ collected reports of 38 cases of metastatic carcinoma of the gallbladder in which the incidence of cholelithiasis was only 8 per cent, a figure which approaches the incidence of simple cholelithiasis for this age group. Such observations are prima facie evidence that cholelithiasis predisposes to carcinoma of the gallbladder.

Kazama²⁶ in 1922 was the first to test this relation experimentally. He inserted foreign bodies (stones, sutures and mucosa) into the gallbladders of guinea-pigs and found that after a time carcinoma of the gallbladder, even a metastasizing tumor, developed in some of the animals. His researches stimulated a series of similar experiments by Leitsch,²⁷ Clemente²⁸ and others, the results of which are controversial. Lazarus-Barlow,²⁹ who demonstrated radio-activity in the salts of some gallstones, suggested that this radiation caused the malignant growth.

Burrows³⁰ recently reviewed the subject of the experimental production of carcinoma of the gallbladder. After cautious study, he concluded that cancer has not been produced and that the numerous attempts have failed to demonstrate any carcinogenic substance in gallstones. Foreign bodies in the gallbladder stimulate proliferative reactions in the mucosa that simulate cancer but do not cross the indefinite boundary between metaplasia and neoplasia.

Relation of Infection.—A pathologic change more constant than cholelithiasis is infection. In cases of carcinoma in the early stage in which only a small portion of the mucosa is invaded by tumor, there are always varying degrees of subacute or chronic infection with fibrous thickening of the free portion of the organ, depicting a long-standing inflammatory process. Consequently, all recent observers have accepted infection as a precursor of carcinoma.

Relation of Papillomas.—In 1910 MacCarty³¹ emphasized the frequency of benign papillomas of the gallbladder, describing the con-

25. Graham, E. A.: The Prevention of Carcinoma of the Gallbladder, *Ann. Surg.* **93**:317-322, 1931.

26. Kazama, Y.: The Studies on the Artificial Production of Tumors in the Viscera, *Japan M. World* **2**:309-312, 1922.

27. Leitsch, A.: Gallstones and Cancer of the Gall-Bladder, *Brit. M. J.* **2**: 451-454, 1924.

28. Clemente, G.: Tumori sperimentali della colecisti da catrame, *Arch. ital. di chir.* **17**:613, 1927.

29. Lazarus-Barlow, W. S.: An Attempt at the Experimental Production of Cancer by Means of Radium, *Proc. Roy. Soc. Med. (Sect. Path.)* **11**:1, 1917.

30. Burrows, H.: An Experimental Inquiry into the Association Between Gallstones and Primary Cancer of the Gallbladder, *Brit. J. Surg.* **20**:607-629, 1933.

31. MacCarty, W. C.: Pathology of the Gallbladder and Some Associated Lesions, *Ann. Surg.* **51**:651-669, 1910.

dition as "cholecystitis catarrhalis papillomatosa." He considered this a type of "strawberry gallbladder," since many of the papillomas contained deposits of cholesterol. This condition has received further recognition from Mayo,³² Keene,³³ Mölle³⁴ and Abell.³⁵

Malignant degeneration in papillomas has been reported by Ringel,³⁶ Pels-Leusden³⁷ and others. Illingworth²¹ thought that papillomas rarely show precancerous changes. Phillips,³⁸ in a series of 500 cases, found but 1 with carcinoma. In this case the papillomas were multiple and all benign, while the carcinoma was solitary and malignant throughout. He could not, then, prove the pathogenesis to be malignant degeneration.

The lesion described by MacCarty occurs relatively early in the course of disease of the gallbladder. All such cases show some infection in the mucosa. Stones were present in 26.8 per cent of Phillips' cases. Because of the deposits of cholesterol, it is likely that many more eventually would have formed stones. The presence of papillomas is ample evidence of the epithelial proliferative power. One cannot, then, deny that the papillomatous gallbladder has the capacity of forming carcinoma, for infection, stones and the power to proliferate are the most common etiologic factors. All that one can require further than this is the ultimate—a susceptible subject.

PATHOLOGIC PICTURE

The pathologic picture of carcinoma of the gallbladder has been described adequately by Courvoisier,⁸ Kaufmann,³⁹ Ewing⁴⁰ and others. Pathologically, the disease may be divided into two groups: adenocarcinoma and squamous carcinoma. The adenocarcinomas may be

32. Mayo, C. H.: Papillomas of the Gall-Bladder, in *Collected Papers of the Mayo Clinic*, Philadelphia, W. B. Saunders Company, 1915, vol. 7, pp. 249-255.

33. Keene, F. E.: Papilloma of the Gall-Bladder, *Proc. Path. Soc., Philadelphia* **38**:7, 1918.

34. Mölle, H.: Ueber Papillome der Gallenblase, nebst Mitteilung eines selbst beobachteten Falles, *Beitr. z. klin. Chir.* **99**:173-185, 1916.

35. Abell, I.: Papilloma and Adenoma of the Gallbladder, *Ann. Surg.* **77**: 276-280, 1923.

36. Ringel: Ueber Papillom der Gallenblase, *Arch. f. klin. Chir.* **59**:161-166, 1899.

37. Pels-Leusden, F.: Ueber papilläre Wucherungen in der Gallenblase und ihre Beziehungen zur Cholelithiasis und zum Carcinom, *Arch. f. klin. Chir.* **80**:128-160, 1906.

38. Phillips, J. R.: Papilloma of the Gallbladder, *Am. J. Surg.* **21**:38-42, 1933.

39. Kaufmann, E.: *Lehrbuch der speziellen pathologischen Anatomie für Studierende und Aerzte*, ed. 5, Berlin, G. Reimer, 1909, vol. 5.

40. Ewing, J.: *Neoplastic Diseases*, Philadelphia, W. B. Saunders Company, 1931, pp. 736-740.

subdivided into (a) papillary adenocarcinoma, (b) infiltrating adenocarcinoma, (c) scirrhous adenocarcinoma and (d) mucous adenocarcinoma.

Inflammation coupled with the chronic mechanical irritation caused by gallstones produces a variety of reactions in the tissues of the gallbladder. The type of reaction probably determines the type of tumor which is to form. If the submucosa is more responsive to irritation than the mucosa, the resulting papilloma may be composed chiefly of connective tissue elements covered with normal epithelium. In my opinion, this type of papilloma is the least likely to form carcinoma, for the epithelium shows growth restraint under stimulation.

Should the response be an overgrowth of epithelium, simple benign papillomas may develop. With all growth restraint removed and anaplasia in abeyance, the gallbladder may become distended with a bulky, benign papillary growth. Such rare tumors have been described by Sand and Mayer⁴¹ and by Chappet.⁴² They are clinically malignant because of their situation but are pathologically benign. Devic and Gallavardin⁴³ described a case in which the growth extended down into the common duct. In one of the cases in the present series the tumor was definitely of this type, though sufficient connective tissue was present to give it a villous appearance not unlike a bunch of white grapes.

ADENOCARCINOMA

Papillary Adenocarcinoma.—If anaplasia is present, the papillary overgrowth of epithelium is malignant, resulting in papillary adenocarcinoma of the gallbladder. This is a common type; in 12 per cent of the cases at the New York Hospital the condition is of this nature. The tumor is composed of multiple papillary stalks of connective tissue covered with atypical cylindric cells and infiltrated by secondary alveoli lined with cuboidal cells. The tumor may be bulky, sometimes distending the gallbladder or obstructing the cystic duct. Ulceration may limit its growth into the lumen. In general, this type of tumor is slower growing, less malignant and more bulky than any other. Infiltration is slight, metastases are late and infection is marked. Operation is performed in a good many cases for acute or subacute cholecystitis.

41. Sand, R., and Mayer, L.: Transformation de la vésicule biliaire tout entière en un kyste papillaire. Arch. de méd. expér. et d'anat. path. **23**:523-528, 1911.

42. Chappet, V.: Cancer épithélial primitif du canal cholédoque; hydropisie de la vésicule; ictère par rétention; absence de généralisation; cachexie progressive, Lyon méd. **76**:145-157, 1894.

43. Devic and Gallavardin, L.: Etude sur le cancer primitif des canaux biliaires, cholédoque, hépatique et cystique, Rev. de méd. **21**:557, 1901.

Infiltrating Adenocarcinoma.—If anaplasia is marked and ulceration present from the start, papillary overgrowth may never have a chance to occur. The result is infiltrating adenocarcinoma, which formed 56 per cent of this series. The tumor consists of infiltrating atypical alveoli and pseudo-alveoli and does not increase the bulk of the organ. It rapidly invades all layers of the gallbladder and the liver and through adhesions, the duodenum, stomach, colon, omentum and peritoneum. Metastases occur early to the regional nodes and liver. It is in this group that metastases occasionally give rise to the first clinical manifestations of disease.

Scirrhus Adenocarcinoma.—This tumor also is of the infiltrating type of adenocarcinoma, the difference being the extensive growth of new cellular connective tissue. Whether this desmoplastic quality is reaction to preexisting inflammation or to the growth of the tumor is disputed. The picture is that of extensive fibrosis infiltrated by strands of atypical epithelial cells which tend to form alveoli. The fibrosis can be considered a defense reaction or evidence of immunity to the cancerous growth which never quite succeeds in strangulating the malignant cells. Like fibrous tissue elsewhere, it contracts with age, often resulting in obliteration of the cavity of the gallbladder. It may produce an hour-glass deformity of the organ or squeeze stones into the common duct. The only remnant of the gallbladder may be a solid knot of scar tissue with a central calculus on the inferior surface of the liver. Should the tumor arise at the neck it may cause obstruction of the cystic duct and also empyema or mucocele of the gallbladder. In 25 per cent of the cases in the present series the growth was a scirrhus adenocarcinoma.

Mucous Adenocarcinoma.—In any of the three types mentioned, mucous degeneration may occur in one part or all of the tumor. It is a regressive change due to overgrowth of the mucous constituents of the gallbladder. Should mucous degeneration be a primary feature of the tumor, there may result extensive secretion of mucus and a bulky gelatinous mass which distends the gallbladder. Because of the friability of this tumor, there is a tendency to early perforation of the organ and extension of the lesion to the peritoneum. Twelve per cent of the cases in the present series showed isolated foci of mucous degeneration. There were 2 cases of bulky mucous adenocarcinoma.

SQUAMOUS CELL CARCINOMA

Neither during its development from the primitive gut nor in the adult form is there a vestige of squamous epithelium in the gallbladder. The occurrence of definite squamous cell carcinoma must, then, be the

result of metaplasia. This belief is borne out by the occasional presence in the mucosa of the gallbladder of local or general leukoplakia. Lubarsch⁴⁴ found a squamous cell papilloma the size of a bean. Further irritation may initiate malignant changes. A portion or all of the tumor may have squamous characteristics. Deetz⁴⁵ reported pearl formation, but keratinization is not a marked feature.⁴⁶ The gross picture is not unlike that of scirrhus adenocarcinoma. Metastases may have the same squamous characteristics or may revert to the adenocarcinomatous type. The clinical course is like that of the scirrhus or infiltrating types. It is the least common type of carcinoma of the gallbladder. But 1 example was seen in the cases at the New York Hospital.

SITE OF ORIGIN

Carcinoma may occur in any portion of the epithelium of the gallbladder. In the majority of cases (56 per cent in the present series) the growth is so extensive that it is impossible accurately to determine the origin. Cases in which the growth is less advanced show that the tumor generally arises at the fundus or in or near the neck of the organ.

It is estimated that in from 80 to 90 per cent of the cases the growth originates in the fourth of the mucosal area represented by the dome and the neck of the gallbladder. In the remaining 10 to 20 per cent it arises at some site about the lateral walls.

The explanation of this unequal distribution harks back to the etiologic rôle of calculi. Gravity and efforts of the organ to empty itself of stones cause greater irritation to the extremities than to the walls of the organ.

In the present series, the original site of the tumor could be determined in but 21 cases. In 12 of these it was at the fundus, and in 9, at or near the neck. No discrete tumors were found on the peritoneal or hepatic walls.

Obviously, the site of the tumor may influence the course of the disease and the resulting clinical picture as much as the type of tumor. A growth may exist at the fundus and not give rise to symptoms until dissemination is advanced. A scirrhus or papillary tumor at the neck, on the contrary, may cause obstruction of the cystic duct relatively

44. Lubarsch, Otto: *Pathologische Anatomie und Krebsforschung*, in *Arbeiten aus der pathologisch-anatomischen Abteilung des königl. hygienischen Instituts zu Posen*, Wiesbaden, 1901, p. 205.

45. Deetz, E.: Vier weitere Fälle von Plattenepithel-Krebs der Gallenblase, ein Beitrag zur Frage der Epithel-Metaplasie, *Virchows Arch. f. path. Anat.* **164**:381-405, 1901.

46. Kodama, Shuichi: The Lymphatics of the Extrahepatic Biliary Passages, *Surg., Gynec. & Obst.* **43**:140, 1926.

early. A tumor on the hepatic wall of the gallbladder, by its very position, is likely to extend into or metastasize to the liver earlier than one on the free peritoneal wall, while the latter may early involve adhering peritoneal organs.

MODE OF EXTENSION

From its original site in the mucosa, a carcinoma disseminates to involve the whole gallbladder and other organs. In general, this is accomplished by local extension, lymphatic metastases and blood-borne metastases.

The lymphatics of the gallbladder consist of a rich plexus of lymph channels in the subepithelial layer and a second plexus of lymph channels in the subserosal layer, which communicate by numerous short anastomotic branches, perforating the muscular layer. The subserosal plexus in turn is collected into several main lymphatic vessels, which follow the cystic artery rather closely down onto the neck of the organ, where they terminate in the cystic node ("signal gland" of Lund). From there the lymphatics extend chiefly to the chain of mesenteric nodes which lie beside the common duct and portal vein, up to the hilus of the liver. This chain of nodes also receives branches from the pancreatic nodes, the aortic nodes and the second portion of the duodenum. Kodama⁴⁶ has demonstrated a direct lymphatic connection between the gallbladder and the first portion of the duodenum in dogs. Of great importance is the original work of Poirier and Charpy⁴⁷ and of Sudler,⁴⁸ which demonstrated an intimate connection between the lymphatics of the liver and those of the subserosal layer of the gallbladder. This work is questioned by many, but it is accepted by Graham⁴⁹ and is borne out by clinical observations.

Local extension is by far the most common method of dissemination. Infiltration first takes place through the layers of the gallbladder itself, being facilitated by the cholecystic lymphatics. Because of the arrangement of the lymphatics, the infiltrating tumor tends to encase the gallbladder on all sides early, resulting in a hard, thickened organ, which is often contracted.

The liver is involved earlier and more frequently than any other organ. This is accomplished in four ways: 1. The most common route is direct extension to the adjacent right lobe of the liver facilitated by the direct connection between the hepatic lymphatics and the subserosal

47. Poirier, P., and Charpy, A.: *Traité d'anatomie humaine*, Paris, Masson & Cie, 1901, vol. 4, p. 814.

48. Sudler, M. T.: The Architecture of the Gallbladder, *Bull. Johns Hopkins Hosp.* 12:126-129, 1901.

49. Graham, E. A.: *Diseases of the Gallbladder and Bile Ducts*, Philadelphia, Lea & Febiger, 1928, pp. 30-34.

lymphatic plexus of the gallbladder. The process reduces the gallbladder and the adjacent portion of the liver to a hard knot of lobulated tumor tissue and seldom occurs until the gallbladder itself is completely infiltrated. Direct extension to the liver occurred in 66 per cent of the cases at the New York Hospital. 2. Hepatic metastases may occur through these same lymphatics. They usually are associated with direct extension, are multiple and small and on or near the surface of the right lobe of the liver in the region of the gallbladder. This type of metastases to the liver occurred in 36 per cent of the cases. In all of these there was also direct extension to the liver. The metastatic nodules varied in size between 2 and 6 cm. 3. Metastases to the liver may also occur through the periportal lymphatics in a retrograde fashion. In such cases there usually is metastatic involvement of the cystic and periportal nodes; the hepatic nodules are deep in the substance of the right lobe or rarely of the left lobe. In 1 case hepatic metastases of this type were present. There was gross involvement of the cystic and periportal nodes. 4. Recently Karlmark⁵⁰ concluded that hepatic metastases tend to localize in the quadrate lobe following the venous drainage of the gallbladder. His study concerns sarcoma as well as carcinoma of the gallbladder. Unquestionably the tumor occasionally may invade veins or arteries and thus give rise to bizarre blood-borne metastases to the liver or to distant organs.

Lymphatic metastases almost invariably involve the cystic nodes (in 52 per cent of the present series) and usually the periportal nodes (in 48 per cent of the series). Beyond the periportal nodes, lymphatic metastases are not uncommonly found in the retroperitoneal nodes about the aorta and about the pancreas (in 19 per cent of the series). The involvement of the periportal and pancreatic nodes may be massive with secondary infiltration of all surrounding structures, giving rise to obstruction of the common duct or portal vein. Occasionally, the portal vein is infiltrated by neoplastic tissue, resulting in portal obstruction or rarely in fatal hemorrhage. Infection may supervene, causing local abscess formation, pylephlebitis, thrombosis of the portal vein, multiple hepatic abscesses or septicemia.

Rarely, the mediastinal, tracheobronchial or supraclavicular nodes may be involved. Cappell and Tudhope⁵¹ reported an unusual case with cervical metastases invading the internal jugular vein upward into the sigmoid sinus and causing hemiplegia. Strangely, there were no symptoms referable to the gallbladder.

50. Karlmark, E.: Die Lokalisationstendenz bei Metastasierung durch die Venen in die Leber, *Acta path. et microbiol. Scandinav.*, supp. 13, 1932, pp. 1-203.

51. Cappell, D., and Tudhope, G.: Primary Carcinoma of the Gall-Bladder with Unusual Metastases, *J. Path. & Bact.* 37:167-168, 1933.

In almost every instance there is infiltration of the peritoneum of the gallbladder, but only in the late stages of the disease is the general peritoneal cavity involved. The mucous type of tumor is most likely to result in generalized peritoneal implants, in which event ascites is common.

Involvement of the omentum is probably next in frequency. This occurs by direct extension rather than by lymphatic spread, for the omentum often is adherent to the gallbladder after inflammation.

As with acute cholecystitis, so with carcinoma, the stomach, duodenum, jejunum or colon may become adherent to the gallbladder and by virtue of contiguity may be secondarily involved by tumor. Obstructive symptoms at one of these points in the gastro-intestinal tract may mask the primary symptoms of disease of the gallbladder.

The gallbladder may perforate into a neighboring viscus, causing a cholecystic fistula. Perforation into the colon occurred in 10 per cent of Musser's ⁷ 100 cases, while in Riedel's ⁵² 77 cases there was perforation into the duodenum in 10 and into the stomach in 5. Rolleston ¹⁶ considered the formation of a fistula less common in cases of carcinoma of the gallbladder than in those of cholelithiasis. In the series of cases at New York Hospital there was but 1 case of duodenal fistula, though tumor had invaded the duodenum in 5 cases, the pylorus in 2 and the hepatic flexure in 3.

Pulmonary metastases are not uncommon; they usually are very small and near the pleura in the lower lobe of the right lung. Their occurrence at this site confirms the view that they find their way from the abdomen through the retrodiaphragmatic lymphatics. Multiple and solitary metastases to other portions of the pulmonary parenchyma occur, however, and are probably blood borne. There were pulmonary metastases in 4 per cent of the series. All were in the lower lobe of the right lung.

Distant metastases are rare, but isolated case reports show that many parts of the body may be involved by secondary tumors. Beadles ⁵³ reported an enormous metastatic tumor of the second rib. Warthin ⁵⁴ discovered a case with cutaneous pigmentation due to metastases to the

52. Riedel, B.: *Zur Diagnose und Therapie des Gallenblasenkarzinomes*, München. med. Wchnschr. **58**:1337-1340, 1911.

53. Beadles, C. F.: *Primary Carcinoma of the Liver (Gallbladder) Associated with a Large Tumor on the Thoracic Wall*, Tr. Path. Soc. London **48**:119, 1897.

54. Warthin, A. S.: *A Case of Primary Adenocarcinoma of the Gall Bladder with Secondaries in Both Adrenals, Melanosis of Skin (Addison's Disease?), Vitiligo, and Hypertrophy of the Pancreas*, Philadelphia M. J. **6**:38, 82 and 120, 1900.

adrenal glands. Osler⁵⁵ described a metastatic nodule in the breast. Wakasugi⁵⁶ found extensive metastatic involvement on the pelvic floor simulating carcinoma of the rectum. Rolleston¹⁶ mentioned a case with metastatic tumor of the spine simulating tuberculosis.

CLINICAL FINDINGS

Since cholecystitis and cholelithiasis so frequently precede carcinoma, the early history in many cases is typical of inflammatory disease of the gallbladder. The first complaint may antedate the symptoms for which the patient seeks relief as long as twenty or thirty years. In other cases there are no manifestations of long-standing disease, yet in many of them gallstones are found. It is known that gallstones do not invariably cause symptoms, but this is not a likely explanation of the lack of early complaints in a large percentage of patients. A more probable reason would appear to be the relative mildness of the early symptoms.

Past History.—In only 52 per cent of the cases in the present series was there a frank history of disease of the gallbladder of long standing, yet in 70 per cent of those in which no such history was elicited stones were found. The past history was typical of intermittent biliary colic in 44 per cent of the forty-eight cases and consisted of flatulent indigestion, epigastric discomfort and intolerance of fatty foods in 8 per cent. The average duration of the past symptoms was eleven and a half years. In 1 case a single attack of painless jaundice occurred three years before the patient's admission, and in another one attack of biliary colic was followed by jaundice thirty years previously. In 3 cases cholecystostomy had been performed for acute cholecystitis associated with stones. In 1 of these cases cholecystostomy was performed three times at intervals of one year, the last operation being performed two years before the present illness. In 1 case a carcinoma developed in the stump of the cystic duct four years after a cholecystectomy for cholelithiasis.

SYMPTOMS OF CARCINOMA

After the onset of carcinoma, the clinical course of cholecystitis and cholelithiasis observed in the past history is usually modified by symptoms referable to the tumor and its growth. The symptoms attributable to carcinoma of the gallbladder are pain associated with nausea, vomiting and anorexia, followed in the course of time by loss of weight and

55. Osler, W.: On the Medical Aspects of Carcinoma of the Breast, *Brit. M. J.* 1:1-4, 1906.

56. Wakasugi, K.: Zur Kenntnis der sekundären Neubildungen der Tuben, *Beitr. z. path. Anat. u. z. allg. Path.* 47:483, 1910.

jaundice of the obstructive type. Some tenderness is usually elicited, and the gallbladder may be palpable as a hard mass in the right upper quadrant. These symptoms will be considered separately in the order of their frequency.

Pain.—The most common symptom in the group of cases was pain. It occurred in 43 of the 48 cases; in 69 per cent it was the first symptom of the disease. Four of the five patients without pain at the time they were seen had had attacks of biliary colic at some earlier period. The only patient in whom pain had never been a feature had an extensive tumor, which infiltrated and obstructed the duodenum.

The pain was almost invariably referred to the epigastrium or the upper right quadrant. A woman of 28 with situs inversus viscerum had pain in the left side due to carcinoma of a left-sided gallbladder. In 2 patients pain in the right upper quadrant was the only symptom.

The pain in these patients was constant, persisting over a period of time as a dull ache, with or without exacerbations of colic. In 54 per cent it was constant and dull, with an average duration of eight weeks. An additional 46 per cent suffered colicky exacerbations.

Loss of Weight.—In 95 per cent of the 48 cases loss of weight was a prominent feature. In 5 it was clearly the first symptom, but in none was it the only symptom. The loss of weight was generally dependent on the severity of the anorexia and the gastro-intestinal disturbance. The average loss of weight was 16 pounds (7.3 Kg.); the greatest loss, 100 pounds (45.4 Kg.).

Anorexia.—This symptom was present in 85 per cent of the cases. Though often severe, it was never the outstanding feature that it is prone to be in carcinoma of the stomach.

Tenderness.—Tenderness in the right upper quadrant or over the mass was found in 73 per cent of the cases. When the tenderness was marked it was associated with more or less rigidity.

Palpable Mass.—A palpable mass was present in 50 per cent of the cases. It was described as firm and tender and varied between 6 and 10 cm. in diameter. In all cases the mass proved to be a carcinomatous gallbladder. In 2 instances the discovery by the patient himself of a mass in the right upper quadrant constituted the first manifestation of the disease.

Edge of the Liver Palpable.—The edge of the liver was palpable in 50 per cent of the cases and descended between 2 and 10 cm. below the costal margin. It could be felt in the majority of patients with jaundice, though only half of these had hepatic metastases; however, some infiltration was always present. In no instance was the liver notably nodular.

Jaundice.—This symptom was present at the time of admission in 48 per cent of the cases, and in 6 it constituted the first symptom. In 4, jaundice associated with loss of weight and anorexia was the only symptom. The average icteric index was 100 and varied between 20 and 240. The average duration of the icterus was five weeks. The jaundice usually was continuous, though in 5 cases it was intermittent, and in 2 others it fluctuated. In all instances it was due not to hepatic metastases but to obstruction of the common duct. The obstruction, in turn, was caused by pressure of metastatic nodes or infiltration by the primary tumor in 91 per cent of the cases. There were but 2 cases of choledocholithiasis. Acholic stools and bile-stained urine accompanied the jaundice in most instances. Pruritus was extremely variable.

Vomiting.—According to the recent history in 45 per cent of the cases vomiting occurred at some time. In 1 it was the first manifestation of the disease. It usually appeared in mild form related to severe pain. In 2 cases, however, it was persistent, severe and the outstanding symptom; in both of these there was duodenal obstruction due to infiltration by the tumor.

Leukocytosis.—Laboratory examination showed leukocytosis to be a variable finding, occurring in 45 per cent of the cases. The average count was 14,500 and was closely related to the extent of the associated infection.

Anemia.—Anemia was not a marked feature in this group of cases. The average hemoglobin content was 74 per cent. In 2 cases of long-standing infection in the gallbladder the readings were below 60 per cent.

Chills and Fever.—These symptoms were marked in but 2 cases; obstructive jaundice was present in both, and at autopsy cholangitis was noted. Fever at some time during the course of the disease was of extremely common occurrence.

ATYPICAL FORMS

Rarely, patients fail to present symptoms referable to the gallbladder, the first clinical manifestations of the disease being due to metastases. In this connection Lancereaux²⁴ described a hepatic form of the disease characterized by belching, vague abdominal pains, enlargement of the liver and slight jaundice, the clinical course of which is essentially that of carcinoma of the liver.

The clinical picture was atypical in 7 of the cases in the present series. Four of these had symptoms of obstruction of the common duct, i. e., painless jaundice with loss of weight and anorexia. In all of these metastatic nodes were obstructing the common duct. Duodenal obstruction was the dominant feature in 2 cases, in both of which vomiting was the outstanding symptom. In 1 case there was biliary colic of short

duration, with a palpable gallbladder, which is consistent with the clinical diagnosis of hydrops. At operation carcinoma was found at the fundus with a stone impacted in the cystic duct.

DIAGNOSIS

The diagnosis of carcinoma of the gallbladder is difficult to establish with certainty. With a past history of biliary colic and a recent illness characterized by steady pain, loss of weight, anorexia, obstructive jaundice and a hard palpable mass in the right upper quadrant, the diagnosis is almost certain. However, only about 30 per cent of the patients presented this combination of clinical findings.

As stated earlier, steady, dull pain in the epigastrium or the right upper quadrant proved to be the most constant symptom. The persistence of this type of pain over a period of weeks is unusual in inflammatory disease of the gallbladder. It is felt, therefore, that the type of pain is the most useful feature in differentiating carcinoma of the gallbladder and the inflammatory diseases with which it is most frequently confused. In the presence of painless jaundice, carcinoma of the common duct, ampulla of Vater or head of the pancreas must be considered. Most ampullary tumors cause occult blood in the stools, while the gallbladder is usually palpable but not tender in cancer of the head of the pancreas.

When the clinical diagnosis is uncertain, the aid of the roentgenologist usually is invoked. In spite of the recent advances in cholecystography, roentgenograms of the gallbladder seldom are of assistance in differentiating inflammatory and neoplastic diseases in this region. The reasons for this are obvious when the extent of the pathologic process in most cases of carcinoma of the gallbladder is taken into account. If sufficient normal mucosa is left to concentrate the dye and thereby render the gallbladder visible in the roentgenogram, the chances are great that calculi will obscure the picture. Often the tumor, by obstructing the cystic duct, prevents the dye from entering the gallbladder.

There are a few recent reports in the literature (notably those of Takerta,⁵⁷ Spitzenberger⁵⁸ and Albrecht⁵⁹) which emphasize the value of the roentgenogram in diagnosing carcinoma of the gallbladder. Kirklin⁶⁰ has discussed the subject recently.

57. Taterka, H.: Cholezytographische Untersuchungen mittels Decholindehnung und Eigelbentlehnung, *Röntgenpraxis* 3:721-731, 1931.

58. Spitzenberger, O.: Zur Diagnose exulzerierender Gallenblasenkarzinome mittels des Röntgenverfahrens, *Wien. klin. Wchnschr.* 46:1421-1423, 1933.

59. Albrecht, H. V.: Die Röntgendiagnostik des Verdauungskanaals, Leipzig, Georg Thieme, 1931.

60. Kirklin, B. R.: Cholecystographic Diagnosis of Neoplasms of the Gallbladder, *Am. J. Roentgenol.* 29:8-16, 1933.

In the present series of 48 cases, cholecystograms were made in only 17; in 9 of these the gallbladder could not be visualized, in 7 there were stones and in 1 the gallbladder was clearly outlined but failed to empty well. In these 17 cases, then, there was evidence of cholecystic disease, but in no instance could a diagnosis of carcinoma of the gallbladder be made by roentgen examination.

TREATMENT AND RESULTS

As in most malignant disease in which early diagnosis is difficult, the results of treatment are not encouraging. Operation was performed in 45 of the series of 48 cases, the various operations being exploratory laparotomy with removal of tissue for biopsy, cholecystectomy, cholecystostomy and gastro-enterostomy.

Exploration and biopsy of the tumor were carried out in 21 cases. In all of these obvious metastases were encountered, and the condition was therefore considered inoperable. Eight of the patients in this group succumbed to operation, a mortality of 38 per cent. In 5, death was due to bleeding in the presence of jaundice. The average duration of life after operation in the 13 survivors was three and one-half months.

Cholecystectomy was done in 16 cases. There were 4 postoperative deaths, a mortality of 25 per cent. In 2 of the fatal cases, the common duct was drained because of jaundice. Five patients presented no evidence of metastases at the time of operation. One of these 5 was known to be alive and well two years later but has since been lost from observation. The remaining 4 patients died, on an average of ten months after operation. There were 7 patients with known metastases who survived operation, but only for an average period of six months.

Cholecystostomy was performed on 6 patients. In all of these there was jaundice. Four died as the result of the operation, a mortality of 66 per cent. Three of the 4 deaths were due to hemorrhage. The 2 survivors died six weeks after operation.

Gastro-enterostomy was done on 2 patients as a palliative procedure for duodenal obstruction caused by tumorous infiltration. One patient died, and the other lived five weeks.

With possible cure in but 1 of 45 cases, the results of operation in this group are extremely poor. Not all authors report such discouraging experiences, however. Webber,⁶¹ in grading Judd and Gray's⁶² cases, mentioned 12 cases in which the patients lived over two years. Magoun

61. Webber, I. M.: Grades of Malignancy in Primary Carcinoma of the Gallbladder, *Surg., Gynec. & Obst.* **44**:756-760, 1927.

62. Judd, S. E., and Gray, H. K.: Carcinoma of the Gall-Bladder and Bile Ducts, *Surg., Gynec. & Obst.* **55**:308-315, 1932.

and Renshaw⁶³ reported 7 cases in which the patients were living five years after operation. There are occasional reports in the literature of remarkable cures⁶⁴ even after resection of adjacent, infiltrated liver.⁶⁵

Five of the 48 patients in this series were free from metastases at the time of admission to the hospital; this confirms the contentions of Graham²⁵ in his excellent paper on the prevention of carcinoma of the gallbladder. He expressed the belief that the most rational attack on the disease is its prevention by removal of the gallbladder early in all cases of cholelithiasis.

Cholecystectomy has become a relatively safe procedure, and the attitude toward it is undergoing a change. Internists are more inclined to advise surgical treatment; patients are submitting to operation earlier in the course of the disease; surgeons are performing early cholecystectomy, with improved results and constantly decreasing mortality. Should this trend persist, carcinoma of the gallbladder may once more become uncommon, being confined to the cases in which the growth fails to give rise to early symptoms referable to the gallbladder.

63. Magoun, J., and Renshaw, K.: Malignant Neoplasm in the Gall-Bladder, *Ann. Surg.* **74**:700-720, 1921.

64. Aiga, Y.: Ueber einen seltenen Fall von operativ dauernd geheilten Gallenblasenkarzinom, *Zentralbl. f. Chir.* **62**:212-215, 1935.

65. Finsterer, H.: Das Karzinom der Gallenblase, *Med. Klin.* **28**:432-436, 1932.

PANCREATIC FISTULA

MEDICAL AND SURGICAL MANAGEMENT

J. M. McCAUGHAN, M.D., PH.D.

AND

B. L. SINNER, M.D.

ST. LOUIS

External fistula of the pancreas may be classified as either complete or incomplete. The former commonly involves the intracapsular portion of the duct of Wirsung in such manner that all the pancreatic juice is lost to the body. This event must be exceedingly rare, as the greater number of the reports encountered in the literature deal with external fistula of the incomplete variety, in which there is only a partial loss of pancreatic juice. Duodenal fistula should be differentiated, from the standpoint of classification, because that condition is complicated by the loss not only of pancreatic juice but of bile and duodenal secretion, and therefore grave and often fatal metabolic disturbances occur as a result. Furthermore, the trypsinogen of the pancreatic fluid becomes activated, and digestion of the tissues of the wound in the nearby region of the fistula rapidly ensues.

Perhaps the earliest case of pancreatic fistula recorded was that of Rommelaere in 1877.¹ Since that time numerous case reports have appeared in the literature. Fistula of the pancreas arises in various ways. It frequently follows a drainage operation on the pancreas for an acute inflammatory condition, but according to Körte,² it is fairly rare as a result of a stab or gun-shot wound of the abdomen. The protected anatomic location of the pancreas is the greatest safeguard against a traumatic insult of this sort,³ but Garré's⁴ famous case of complete transverse division of the body of the pancreas with recovery, after accurate suture of the duct and parenchyma, is classic. Injury to the pancreas may follow an operation on the kidneys, spleen, stomach

From the Department of Surgery, St. Louis University School of Medicine.

1. Rommelaere: Observation d'une fistule pancréatique chez l'homme, Bull. Acad. roy. de méd. de Belgique 9:1023-1042, 1877.

2. Körte, W.: Die chirurgischen Krankheiten und der Verletzungen des Pankreas, in Billroth, T., and Luecke, G. A.: Deutsche Chirurgie, Stuttgart, F. Enke, 1898, no. 45, p. 212.

3. Karewski, F.: Ueber isolierte subkutane Verletzungen des Pankreas und deren Behandlung, Berl. klin. Wchnschr. 44:187-191, 1907.

4. Garré, C.: Totaler Querriss dess Pankreas durch Naht geheilt, Beitr. z. klin. Chir. 46:233-340, 1905.

or duodenum.⁵ In recent years several cases of pancreatic fistula have been reported after partial resection of the pancreas or excision of an islet cell tumor for the relief of hyperinsulinism.⁶

Fistula may also follow an operation for calculi of the pancreatic duct, but probably the commonest source is a cyst of the pancreas. It is seldom possible to extirpate such a cyst because of the difficulty of securing a satisfactory line of cleavage for dissection between the walls of the cyst and the adjacent organs, namely, the stomach, colon, great vessels and omentum. Marsupialization or drainage by tube is most often resorted to, and discharge of pancreatic juice for a variable period usually follows. Judd, Mattson and Mahorner,⁷ in a report of thirty-three cases of pancreatic cyst treated by marsupialization, stated that the discharge continued for a period of from a few weeks up to two years. In none of their cases was further treatment necessary.

The recognition of uncomplicated pancreatic fistula is not difficult. Examination of the fluid for its reaction and enzyme content establishes the diagnosis. Duodenal fistula may be differentiated by the additional presence of bile and by the erosion of the margins of the wound.⁸ Greater difficulty may be experienced in recognizing a pancreatic fistula when it is associated with a biliary fistula, as pointed out by Popper.⁹

The treatment of complete external pancreatic fistula is complicated first by the necessity of restoring pancreatic juice to the body in sufficient quantity and before serious physiologic disturbances have taken place. Hartmann and Elman¹⁰ and McCaughan¹¹ have demonstrated some of the factors concerned in the mechanism of death from total pancreatic fistula in experimental animals, and McCaughan has noted the beneficial action of the daily administration of sodium chloride intravenously in prolonging the life of an animal with a fistula

5. Mayo, W. J.: The Surgery of the Pancreas, *Ann. Surg.* **58**:145-150, 1913. Young, H., and Davis, David M.: *Young's Practice of Urology*, Philadelphia, W. B. Saunders Company, 1926, vol. 2, p. 738.

6. Whipple, A. O., and Frantz, V. K.: Adenoma of Islet Cells with Hyperinsulinism: A Review, *Ann. Surg.* **101**:1299-1335, 1935.

7. Judd, E. S.; Mattson, H., and Mahorner, H. R.: Pancreatic Cysts: Report of Forty-Seven Cases, *Arch. Surg.* **22**:838-849 (May) 1931.

8. Garis, R. W., and Merkel, W. C.: The Symptom-Complex of Complete External Pancreatic Fistula: Report of a Case, *Surg., Gynec. & Obst.* **59**:590-597, 1934.

9. Popper, H. L.: Pankreasfermente in der Galle, *Zentralbl. f. Chir.* **56**: 2515-2517 (Oct. 5) 1929.

10. Hartmann, A. F., and Elman, R.: Effects of the Loss of Gastric and Pancreatic Secretions and Methods for Restoration of Normal Conditions in the Body, *J. Exper. Med.* **50**:387-405, 1929.

11. McCaughan, J. M.: Experimental Studies on the External Secretion of the Pancreas with Special Reference to the Effect of Its Complete Loss by Permanent Pancreatic Fistula, *Am. J. Physiol.* **97**:459-466, 1931.

of this type. Furthermore, the latter showed that pancreatic juice administered by gastric intubation could improve markedly the condition of an experimental animal practically moribund from the effects of long-continued total loss of pancreatic juice. The serious disturbance in the chemistry of the blood, viz., chlorides, carbon dioxide-combining power and the blood urea, were quickly restored to normal by this means. Cathala and Sèneque¹² were able to secure improvement in a patient with a pancreatic fistula by returning the pancreatic juice by intubation. It is interesting to note, however, that in animals death followed only in case of total fistula; when grave symptoms failed to develop, the fistula was shown subsequently to have been subtotal, and the animals frequently exhibited no untoward results whatever.

The treatment of pancreatic fistula is secondarily concerned with the attempts at closure of the fistulous tract. Conservative means should always be adopted in the beginning. The clinical investigations of Wohlgemuth¹³ have laid the basis for this line of treatment, which consists in the administration of a diet low in carbohydrates and rich in alkaline foods and large doses of sodium bicarbonate. Belladonna, or rather atropine, was first recommended by Hartmann^{13a} in 1924. According to others who later used atropine, the results were negligible. Wohlgemuth based his therapeutic regimen on the investigations of Pavlov,¹⁴ who had noted that entrance of the acid gastric juice into the duodenum invariably provoked an increase in the flow of pancreatic juice. Wohlgemuth's measures were therefore designed to inhibit the rate of pancreatic secretion as much as possible. Heineke,¹⁵ Hohmeier¹⁶ and Schmidt¹⁷ obtained satisfactory results by using Wohlgemuth's regimen in cases of their own. Heineke, in addition, advocated the aspiration of the fistula by means of a catheter and suction pump.

12. Cathala, J., and Sèneque, J.: *Fistula pancréatique: Réinjection du suc pancréatique: amélioration, pancréatico-gastrostomie, guérison*, Presse méd. **38**: 1534-1537 (Nov. 12) 1930.

13. Wohlgemuth, J.: (a) *Untersuchungen über den Pankreassaft des Menschen*, Biochem. Ztschr. **2**:350-356, 1907; (b) *Zur Therapie der Pankreasfistel nebst Bemerkungen über den Mechanismus der Pankrasssekretion während der Verdauung*, Berl. klin. Wchnschr. **45**:389-393, 1908; (c) *Beitrag zur funktionellen Diagnostik des Pankreas*, ibid. **47**:92-95, 1910.

13a. Hartmann, M., in discussion on Barthélemy, M.: *Pancréatite aiguë sans stéatonecrose*, Bull. et mém. Soc. nat. de chir. **50**:408, 1924.

14. Pavlov, I. P.: *The Work of the Digestive Glands*, translated by W. H. Thompson, ed. 2, London, C. Griffin & Co., 1910, p. 266.

15. Heineke, H.: *Zur Behandlung der Pankreasfisteln*, Zentralbl. f. Chir. **34**: 265-296, 1907.

16. Hohmeier, F.: *Isolierte subkutane Querzerreissung des Pankreas durch Operation geheilt*, München. med. Wchnschr. **54**:2036-2037, 1907.

17. Schmidt, W.: *Ein Fall von Totalexstirpation einer Pankreaszyste*, München med. Wchnschr. **54**:2480-2482, 1907.

Kroiss¹⁸ recommended the administration in 50 Gm. doses, by mouth or by rectum, of a water-free product prepared by the digestion of meats and consisting largely of the amino-acids thus produced. (The specific product employed [erepton] is no longer on the market.) Ortlich¹⁹ injected astringents and corrosives, such as tincture of iodine, silver nitrate and zinc chloride. Potter²⁰ applied tenth-normal hydrochloric acid to the fistulous tract by means of a dropper and between times maintained pledgets of gauze soaked in a solution of peptone in the cutaneous opening of the fistula. The use of high voltage roentgen therapy was reported as successful by Culler²¹ in the cases of two soldiers with pancreatic fistula. In each case the fistula was said to have closed completely after five irradiations. Orndoff, Farrell and Ivy,²² on the other hand, studied the effects of roentgen therapy on the pancreas in laboratory animals and concluded that while the pancreas could be temporarily injured, its power of regeneration later on over-compensated, and the total output of ferments might become even greater than normal. Our own experience in giving high voltage roentgen therapy to a patient with a pancreatic fistula and a cyst following partial pancreatectomy for hyperinsulinism (to be reported elsewhere) is in accord with the conclusions of Orndoff, Farrell and Ivy. We exposed the left upper quadrant of the abdomen to a current of 200 kilowatts and 5 milliamperes for fifteen minutes at a time, giving a total exposure of seventy-five minutes. There was no noticeable improvement, and surgical incision and drainage later became imperative.

If these conservative methods fail after trial for a reasonable period, radical measures should then be considered. The excision or extirpation of the entire fistulous tract for obvious reasons is rarely possible. In 1905 Doyen²³ reported the first instances of successful implantation of the pancreatic duct into the greater curvature of the stomach after resection of the papilla of Vater for carcinoma. Kausch²⁴ in 1909 reported the successful implantation of the stump of the pancreas into the duodenum after resection of a carcinoma of the papilla of Vater.

18. Kroiss, F.: Ein Beitrag zur Behandlung der subkutanen Duodenum-und Pankreaszerreissung, Beitr. z. klin. Chir. **76**:477-495, 1911.

19. Ortlich, cited by Kleinschmidt.²¹

20. Potter, C.: Treatment of Duodenal, High Intestinal and Pancreatic Fistulas, J. Missouri M. A. **29**:374-378, 1932.

21. Culler, R. M.: Cure of Pancreatic Fistula by the Roentgen Ray, J. A. M. A. **75**:20 (July 3) 1920.

22. Orndoff, B. H.; Farrell, J. I., and Ivy, A. C.: Studies on the Effect of Roentgen Rays on Glandular Activity: V. The Effect of Roentgen Rays on External Pancreatic Secretion, Am. J. Roentgenol. **16**:349-354, 1926.

23. Doyen, cited by Kleinschmidt.²¹

24. Kausch, W.: Die Resektion des mittleren Duodenum: Eine typische Operation, Zentralbl. f. Chir. **36**:1350-1376, 1909.

The experimental work of Coffey,²⁵ Desjardins²⁶ and von Fáykiss²⁷ on pancreatico-enterostomy was an important forward step in this difficult field of surgical technic. After the work of Doyen and Kausch on the transplantation of the pancreatic duct after resection of the papilla of Vater for carcinoma, others began to utilize the principle of this method in dealing with intractable fistula of the pancreas, particularly Jedlicka²⁸ (1921), Lorenz²⁹ (1921), Hammesfahr³⁰ (1923), Kleinschmidt³¹ (1925), Corachan³² (1924), Cathala and Sèneque¹² (1930) and Janes³³ (1934).

The technic consists in making a careful dissection of the fibrous fistulous tract until a sufficient length has been mobilized. This may then be implanted without tension into the nearest portion of the upper part of the gastro-intestinal tract, preferably the stomach. A tag of fat from the round ligament or the gastrocolic or gastrohepatic omentum or even a free graft of fat is stitched about the site of implantation to protect the line of suture against leakage. A small drainage tube is placed near the site of operation, and the abdominal wound is closed in the usual manner.

The entrance of pancreatic juice into the stomach seems to have no deleterious effect on gastric digestion, according to Grey³⁴ and Tripodi and Sherwin,³⁵ who investigated this problem in dogs. Ascending infection by way of the duct, even when the implantation was made into the descending portion of the colon of dogs, did not take place. In Kausch's case of pancreaticoduodenostomy for carcinoma of the papilla of Vater clinical evidence of freedom from ascending pancreatic infection is afforded. The patient died one year after operation, and the

25. Coffey, R. C.: Pancreato-Enterostomy and Pancreatectomy, *Ann. Surg.* **50**: 1238-1264, 1909.

26. Desjardins, cited by Kleinschmidt.³¹

27. von Fáykiss, F.: Ueber experimentelle Pankreasresektion und Pankreatoenterostomie, *Beitr. z. klin. Chir.* **84**:188-200, 1913.

28. Jedlicka, R.: Zur Operation der Pankreas Kysten, *Zentralorg. f. d. ges. Chir.* **16**:153, 1922.

29. Lorenz, H.: Kasuistische Beiträge Zur Pankreas-und zur Gallenchirurgie, *Wien. klin. Wchnschr.* **34**:339-340, 1921.

30. Hammesfahr, C.: Zur Behandlung von Pankreasfisteln, *Zentralbl. f. Chir.* **50**:1758-1759, 1923.

31. Kleinschmidt, O.: Behandlung der Fisteln des Pankreas und des Ductus pancreaticus, *Arch. f. klin. Chir.* **135**:363-372, 1925.

32. Corachan, M.: Sur le traitement des fistules pancréatiques, *Presse méd.* **36**:1394-1397 (Nov. 3) 1928.

33. Janes, R. M.: Pancreatic Fistula: Report of a Case; Cure by Pancreato-Gastrostomy, *Brit. J. Surg.* **22**:296-300, 1934.

34. Grey, E. G.: Diversion of the Pancreatic Juice, *J. Exper. Med.* **26**:825-839, 1917.

35. Tripodi, A. M., and Sherwin, C. J.: Experimental Transplantation of the Pancreas into the Stomach, *Arch. Surg.* **28**:345-356 (Feb.) 1934.

pancreas appeared to be quite normal at necropsy. The mucous membrane of the duodenum had covered the stump of the pancreas up to the opening of the duct, which was about the size of a goose-quill.

The following is a report of a case of pancreatic fistula in which the fistula was transplanted into the stomach.

REPORT OF A CASE

A. F., a white man 49 years of age, a molder, was admitted to the Firmin Desloge Hospital on Jan. 15, 1936. He was referred to one of us (McCaughan) for the surgical closure of a pancreatic fistula, which had followed a Billroth II type of gastric resection. The history is as follows: Nine months prior to the present admission to the hospital the patient was admitted to another institution, complaining of a dull aching pain in the epigastrium of two years' duration. By January 1935 the pain, which came on rather promptly after meals, had become severe, and was accompanied by nausea and vomiting. There had been a loss of 35 pounds (15.9 Kg.) in weight during the preceding twelve months. The nonprotein nitrogen content of the blood was 85.7 mg. per hundred cubic centimeters. Roentgenographic examination of the gastro-intestinal tract at that time revealed an enormously dilated stomach with marked retention and an apparent deformity of the prepyloric segment, which was interpreted as a gastric neoplasm. On March 30 an exploratory operation was performed on the stomach, and a firm thick mass about the size of a hen's egg was found occupying the prepyloric segment of the stomach. There were no palpable lymph glands, but numerous adhesions about the pylorus, duodenum and pancreas were encountered. A posterior gastro-enterostomy was done, and resection was deferred until later because of the poor condition of the patient. On April 15, two weeks afterward, the abdomen was reopened, and the mass in the prepyloric segment of the stomach was found to have shrunk considerably in size. A partial duodenectomy and gastrectomy were done. About one third of the stomach was removed. On the fifth day after operation the patient went into moderate shock, but he rallied after a transfusion of blood. On the eighth day postoperatively a copious watery discharge came from the wound. The patient improved generally thereafter, but the discharge persisted. The flow was practically continuous, but there was a marked increase after meals and a considerable diminution during fasting and at night. On several occasions drainage ceased for periods of from one to five days, but in two such instances bits of silk suture material were extruded from the fistula, and this was followed promptly by the return of drainage. The Wohlgenuth treatment was instituted in an endeavor to bring about healing of the fistula by medical methods, but the results were unsatisfactory. At the time of entry into the Firmin Desloge Hospital the patient stated that the fistula had been draining for more than nine months.

On physical examination the patient appeared markedly undernourished. The teeth were very bad and exhibited a great many caries. Pyorrhea alveolaris was present. There were a few coarse râles in the left side of the upper part of the chest posteriorly, but otherwise the thorax was normal. There was an old median operative scar in the upper part of the abdomen, and about 4 cm. below the xyphoid process there was a tiny cutaneous opening which barely admitted the tip of a small probe. The surrounding skin appeared to be normal. A clear watery fluid was flowing profusely from this opening (fig. 1). A sample of the material was collected for study. The fluid was strongly alkaline. It had a pH of 8.56, and all three of the pancreatic enzymes could be demonstrated. A bacteriologic examination of the fluid showed gram-positive cocci in clusters and gram-

negative rods which fermented lactose. These were probably contaminants from the skin, as neither fistula nor fluid presented any gross evidence of infection. The systolic blood pressure was 125 mg. of mercury and the diastolic, 94 mm. The pulse rate was 72 and the temperature 98 F. The body weight at the time of admission was 118 pounds (53.5 Kg.).

On laboratory examination the urine was normal, except for an occasional leukocyte and erythrocyte microscopically. The blood count showed 7,900 leukocytes and 3,940,000 erythrocytes; the hemoglobin content was 13 Gm. per hundred cubic centimeters. The differential count was normal. The clotting and bleeding time were both normal, as was the clot retraction time. Studies were made of the blood chemistry, with the following results: sugar, 151 mg. per hundred cubic centimeters; non-protein nitrogen, 33 mg.; carbon dioxide content, 49 volumes per cent, and chlorides, 590 mg. A sugar tolerance test by the Shaffer-Hartmann method gave a curve within the normal zone. The Wassermann and Kahn tests of the blood were negative. Examination of the sputum gave negative results. A gastric analysis showed normal free and combined acids. Roentgenograms



Fig. 1.—External fistula of the pancreas, indicated by the pointer.

were taken of the chest, and a fluoroscopic examination of the stomach was made. The roentgenographic examination revealed a moderate degree of peribronchial thickening and emphysema at the bases of both lungs. The interlobular pleura on the right was thickened. A diagnosis of chronic bronchitis was made. The fluoroscopic examination showed a normal esophagus, but the stomach had been resected at its distal third. A gastro-enterostomy stoma was evident 2 inches (5 cm.) proximal to the blind end of the stomach. Barium sulfate passed freely through the stoma.

Physiologic studies were made during the next two weeks, and the responses to various excitatory and inhibitory drugs and foodstuffs were determined. These results will be reported elsewhere. On two occasions prior to operation there was a temporary cessation of drainage, followed by headache, nausea, general malaise and an elevation of temperature to 102 F. These symptoms cleared up quickly with the return of drainage. No reason could be advanced to explain this apparent retention of pancreatic juice.

On Feb. 1, 1936, a transfusion of 600 cc. of citrated blood was given, and on February 10, with the patient under spinal anesthesia, an exploratory operation was performed on the abdomen. The incision was made at the site of the second operative scar, and a small area of skin about the fistula was left in situ. A probe was introduced into the tract as a guide, and the fistula with its attached island of

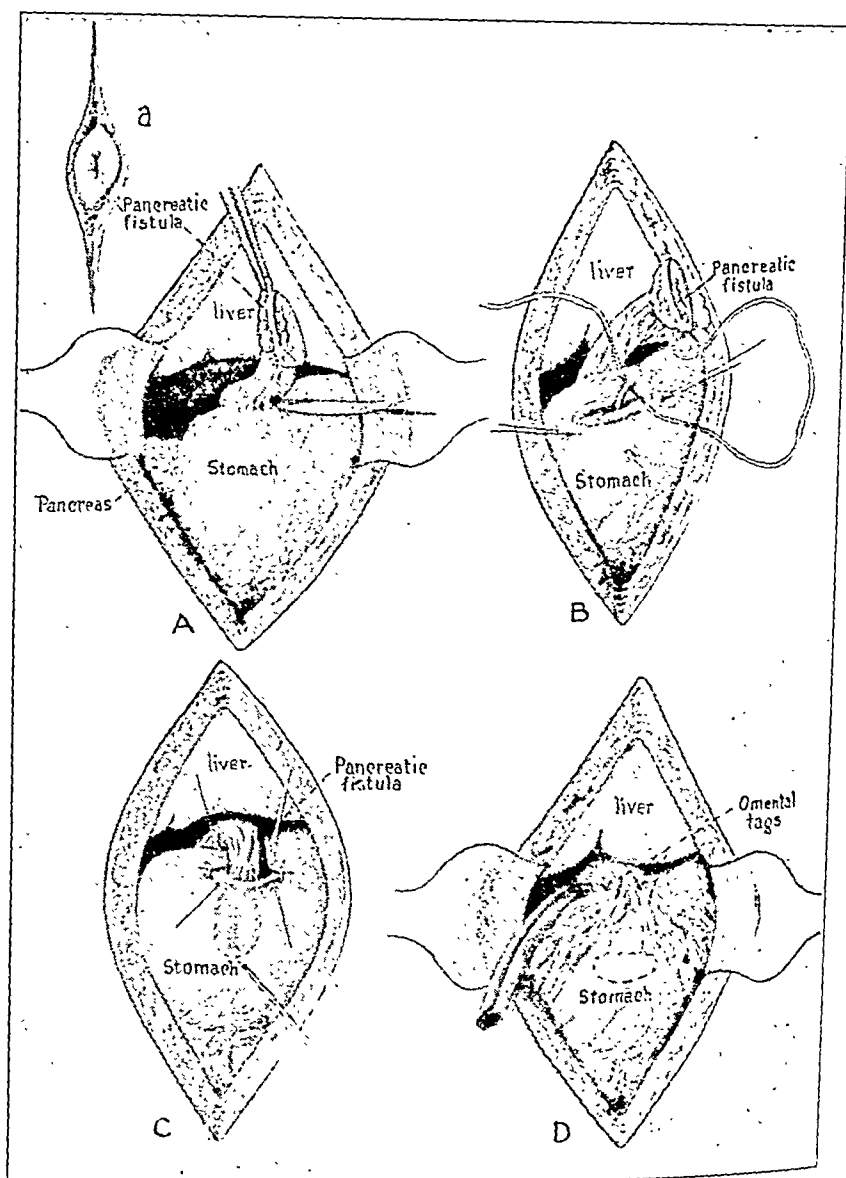


Fig. 2.—The operative technic used in the case reported here. The incision is shown in the small insert (a). An island of skin surrounding the opening of the fistula was left intact. In A, the fistula is being dissected downward. The cicatricial attachment to the lesser curvature and posterior wall of the stomach is being divided by sharp dissection, to obtain complete mobilization. The head of the pancreas is visible in the lower left side of the wound. In B, the stomach has been opened, and the fistula is being prepared for implantation and temporary fixation until gastric closure can be completed. In C, the wall of the stomach is being sutured about the fistula. In this procedure care should be taken not to constrict the tract or to produce angulation. In D, the omental tags of fat are shown stitched about the site of implantation, and the traction suture has been withdrawn, permitting the distal end of the fistula to hang downward. The cuff of skin prevents the fistula from slipping out. A small drain is introduced alongside the site of implantation before the abdominal closure is made.

skin was dissected free and a segment 5 cm. in length mobilized. The fistula measured approximately 1 cm. in diameter. The walls of the tract were rather thin, and some difficulty was encountered in freeing it from the lesser curvature and posterior wall of the stomach. This was accomplished by sharp dissection without injury to the stomach or to the fistula. The adhesions from the two previous laparotomies had walled off the operative field in such a manner as to separate it from the rest of the peritoneal cavity. The fistula was then implanted into the anterior wall of the stomach near the blind end. The technic employed is shown in figure 2. After operation the patient did very well until the fourth day, when a purulent expectoration and a temperature of 104 F. developed. Physical examination of the chest revealed a few moist râles. A roentgenogram showed nothing except a moderate degree of peribronchial thickening as before. These symptoms cleared up rapidly under appropriate treatment. There was

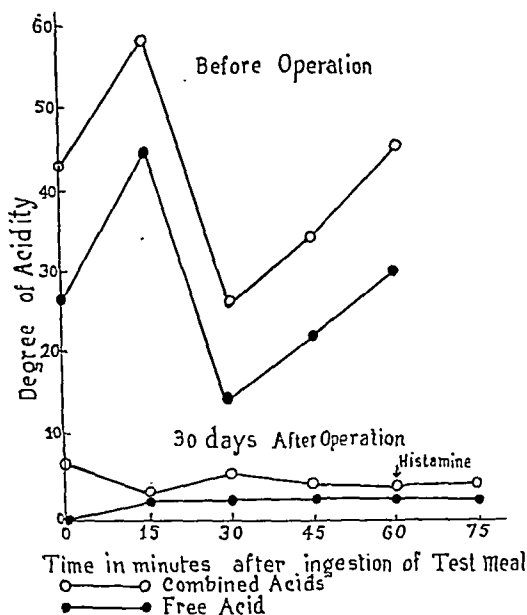


Fig. 3.—Curves showing the degree of gastric acidity before and four weeks after the implantation of the pancreatic fistula into the stomach. The test meal consisted of 240 cc. of 8 per cent ethyl alcohol given by intubation immediately after the removal of the specimen during fasting. In the postoperative analysis, 1 cc. of histamine was given after the fourth, quarter hour interval.

considerable drainage from the wound for the first seventy-two hours. The physical and chemical characteristics of this drainage were identical with those of the fluid from the fistula which was observed previous to operation. At the same time the suture material (no. 2 chromic catgut) gave way apparently as a result of the digestive action of the escaping fluid, and the wound separated completely for a distance of about 4 cm. transversely and about 6 cm. vertically. The base of the wound was seen to be formed by the liver superiorly and the anterior wall of the stomach inferiorly and, covering both, the mesenteric fat which had been drawn up at the time of operation to protect the implanted fistula. Through and through sutures of silkworm gut above and below, however, prevented complete dehiscence. A purulent exudate appeared later, but the leakage

of pancreatic juice ceased abruptly, and with the constant application of gauze soaked in allantoin the infection cleared up gradually, and a growth of healthy granulations soon filled the defect. At the end of four weeks the wound was entirely healed except for a small crust at its center. The patient rapidly regained his weight and strength and felt much improved. Samples of the gastric fluid were also examined for lipase and were found to possess definite lipolytic activity. An index of 0.3 was found when the index for duodenal lipolytic activity by the method employed was from 1.5 to 2 units. A gastric analysis was made for comparison with that obtained before operation, and the degree of acidity was found to have fallen considerably (fig. 3). The diastase in the blood was estimated quantitatively and found to be within normal limits.

The patient was discharged from the hospital on March 15. Two months after operation we were advised that he was gaining in weight and strength. His appetite was fair. There was no dyspepsia and no diarrhea. There was no discharge from the wound, but a small herniation had developed in the lower angle of the wound. This was controlled satisfactorily with a belt.

COMMENT

A case of incomplete pancreatic fistula in which the implantation of the fistulous tract into the stomach was successful, after medical measures had failed to effect healing, is reported. The literature on pancreatic fistula is reviewed, and both conservative and radical methods of dealing with incomplete fistula are discussed in detail. It is difficult to state definitely how long medical measures should be employed before one resorts to surgical treatment. In this instance medical treatment was carried out for perhaps eight or nine months without any significant diminution in the discharge from the fistula. It is questionable whether these procedures can be depended on to bring about a continuous inhibition in the secretion of pancreatic juice. We studied the effect of a variety of drugs and food substances on the activity of pancreatic secretion in this patient, and our results will be published elsewhere. Suffice it to say here that we were able to inhibit or to excite the flow with a number of the substances given, but we question whether these effects could be effectively maintained over long periods of time. Certainly in cases in which there is a well defined fistulous tract with possibly a cicatricial stenosis proximal to it, it would appear futile to continue with the medical regimen. High voltage roentgen therapy had proved unsuccessful in a previous case (to be published elsewhere) and so was not again attempted.

The success of any surgical technic for transplantation will depend on obtaining free mobilization of the fistulous tract and its implantation without tension into the nearest available portion of the upper part of the gastro-intestinal tract, preferably the stomach. It is essential that there are no constrictions or acute angulations, since retention would thereby be favored and the development of a cyst practically a certainty. The tract should not be stitched to the wall of the stomach but should be allowed to find its own proper degree of tension exactly as in the

technic for the production of a perineal urethra. If a suitable island of skin with the fistula opening at the center is left attached, the tract is not likely to slip out, and ultimately that portion beyond the site of union between the intestine and the tract may be expected to slough away as a result of autodigestion. Temporary leakage of gastric and pancreatic juice should be expected, but if the tract is patent it should cease within a few days. The final step in the operative procedure, namely, the utilization of the tags of fat from the adjacent omentum, is an important factor in minimizing the danger of permanent leakage.

The influence on gastric acidity after transplantation is of especial interest. Grey,³⁴ in a series of experiments, transplanted the major pancreatic duct into the wall of the stomach in dogs in which previously a Janeway fistula had been produced. Using a test meal of 70 Gm. of beef and 75 cc. of tap water, he withdrew samples from the fistula at intervals. His results in the main were in agreement with the work of Boldyreff on the self-regulation of the acidity of the stomach and illustrated a remarkable compensatory activity of the gastric glands. He found that the presence of considerable amounts of pancreatic juice in the stomach during digestion led only to a moderate decrease in the acidity level of the ingesta. After months, Grey could find no evidence of inflammatory or degenerative change in the pancreatic glands, although the patency of the ducts could be demonstrated in every instance. The marked decrease in acidity which obtained in our patient differs greatly from Grey's observation on his animals and may be the result of a difference in species. It is more likely due, however, to the fact that the principal acid-forming area of the stomach had been previously extirpated, and the remaining portion was unable to compensate in a normal manner.

In a recent review of the literature on hyperinsulinism, Whipple and his co-workers⁶ reported the occurrence of pancreatic fistula in three of thirty-five cases in which operation was performed. In a similar study, we concluded that pancreatic fistula is more likely to follow the local excision of a pancreatic adenoma than partial resection of the pancreas, in which transverse division and complete-removal of the distal portion are practiced. This conclusion received experimental support from the work of Korovitsky,³⁶ who showed that the ducts were not mere conducting tubes as some supposed, but that they possessed a definite tonus which propelled the pancreatic juice toward the duodenum.

The possibility of inadvertent and even unpreventable trauma to the pancreas during certain intra-abdominal operations should be kept in mind. Such injuries may go unrecognized at the time, but if the surgeon is aware of having injured the pancreas, there is the choice of several

36. Korovitsky, L. K.: The Part Played by the Ducts in Pancreatic Secretion, *J. Physiol.* **57**:214-233, 1923.

procedures, depending, of course, on the location and extent of the wound in the pancreas. In superficial injuries the wound may be closed with a few interrupted sutures and a small drain introduced to the site of the injury before the abdomen is closed. In the case of a more extensive injury the surgeon may elect to do nothing and adopt a policy of watchful waiting with an idea of dealing with complications if and when they occur, or in cases in which the injury is located in the body or tail, he may attempt to circumvent trouble by removing the involved segment and the distal portion of the pancreas. If the major pancreatic duct were divided in the head or in the body, for example, one might attempt to resuture it, as in Garriè's classic case. Perhaps the simplest step of all with injuries situated in the body or tail would be to ligate the pancreas securely at the site of injury. The ensuing atrophy of the acinous cells proceeds rapidly without evident clinical disturbance in experimental animals in which the pancreatic ducts have been divided between ligatures. The islet tissue remains intact, and no interference with carbohydrate metabolism occurs. The digestive disturbances which follow insufficiency of the external pancreatic secretion are the result of the excessive loss of fat and nitrogen in the stools. This loss can now be fairly well controlled by the administration of certain vegetable diastases.³⁷ Drainage should be instituted before closure of the abdomen, in any event, particularly if nothing else can be done at the time, as the avoidance of retention and subsequent pancreatic cyst formation would seem to be especially desirable.

The likeliest sources of danger in abdominal operations are, in the order named: operations on the stomach and duodenum, operations on the biliary tract, operations on the spleen, operations on the kidneys, operations for retroperitoneal tumor and operations on the adrenal glands.

CONCLUSION

External fistula of the pancreas may be complete or incomplete. The incomplete type is the more common as well as the least serious. The treatment of incomplete pancreatic fistula is at first medical, and the basis of such management has been discussed.

The surgical treatment is indicated when conservative measures fail after a reasonable period to bring about definite and continued improvement. The surgical treatment consists in the implantation of the fistula in some readily accessible portion of the upper part of the gastrointestinal tract.

A case of an incomplete pancreatic fistula in which successful transplantation of the fistula into the stomach was done is reported in detail, and the literature is reviewed.

37. Whipple, A. O.; Parsons, W. B., and Mullins, C. R.: Treatment of Carcinoma of the Ampulla of Vater, *Ann. Surg.* **102**:763-779, 1935.

PHYSIOLOGIC AVAILABILITY OF FLUIDS IN SECONDARY SHOCK

HARRY A. DAVIS, M.D.

WASHINGTON, D. C.

The central factor in the production of traumatic shock is the reduction of the volume of blood. The exact mechanism of the oligemia occurring in shock is debatable, but at the present time most consideration has been given to three hypotheses. According to the first, vasotropic substances are formed in the area of injury and are absorbed into the general circulation, producing a marked fall in the blood pressure and an increase in the permeability of the capillaries. As a result, blood and blood plasma pass out into the extravascular tissues, and a reduction in the volume of blood takes place (Cannon,¹ Cannon and Bayliss² and Grunke and Haring³).

Subsequent observers, however, have been unable to obtain convincing evidence of the presence of such toxic products either in the area of injury (Blalock,⁴ Parsons and Phemister⁵ and Simonart⁶) or in the blood stream of human beings suffering from shock (Schneider⁷ and Herbst⁸).

According to the second hypothesis, the reduction in the volume of blood may be satisfactorily accounted for by a loss of plasma and blood

From the Department of Surgery, the University of Chicago, and the Department of Pathology, the George Washington University.

1. Cannon, W. B.: Experimental Traumatic Shock: Evidence of a Toxic Factor in Wound Shock, *Arch. Surg.* **4**:1 (Jan.) 1922.

2. Cannon, W. B., and Bayliss, W. M.: Note on Muscle Injury in Relation to Shock, Reports of the Special Investigation Committee on Surgical Shock and Allied Conditions, Medical Research Committee, London, His Majesty's Stationery Office, 1919, p. 19.

3. Grunke, W., and Haring, W.: Das Verhalten der Blutmenge beim experimentellen Shock, *Ztschr. f. d. ges. exper. Med.* **79**:763, 1931.

4. Blalock, A.: Experimental Shock: Cause of Low Blood Pressure Produced by Muscle Injury, *Arch. Surg.* **20**:959 (June) 1930.

5. Parsons, E., and Phemister, D. B.: Haemorrhage and "Shock" in Traumatized Limbs: Experimental Study, *Surg., Gynec. & Obst.* **51**:196, 1930.

6. Simonart, A.: Etude expérimentale sur la toxémie traumatique et la toxémie des grands brûlés, *Arch. internat. de pharmacodyn. et de thérap.* **37**:269, 1930.

7. Schneider, H.: Ueber das Vorkommen und über die Bedeutung von Gewebsgiften bei Shockzuständen des Menschen, *Deutsche Ztschr. f. Chir.* **229**:343, 1930.

8. Herbst, R.: Experimentelles zur Entstehung des traumatischen Shocks, *Arch. f. klin. Chir.* **176**:98, 1933.

into the traumatized region (Blalock,⁴ Parsons and Phemister⁵ and Herbst⁶). The basis of the third point of view is that a prolonged overactivity of the sympathetic nervous system is capable per se of reducing the volume of blood to a shock level (Freeman⁹ and Malcolm¹⁰). This conclusion followed the observation of a diminished volume of blood in decorticate animals exhibiting sham rage and after prolonged injections of epinephrine. In both instances a hyperactivity of the sympathetic nervous system was readily demonstrable.

Whatever may be the mode of its production, the oligemia causes widespread physiologic effects, in particular an oxygen want which is directly proportional to the reduction in the volume of blood. Even a small hemorrhage and minor grade of shock induces a considerable diminution in the volume flow of blood to peripheral organs, amounting in certain instances to a decrement of as much as 80 per cent (Gesell¹¹). The administration of fluid increases the flow of blood through peripheral blood vessels, even though the fluid possesses no oxygen-carrying properties. However, as will be shown later, an increased volume flow to the periphery does not result, of necessity, in an increased utilization of oxygen by anoxic tissues.

FLUIDS IN SHOCK

In evaluating the fluid therapy of shock, two questions arise: 1. How adequate are fluids in the treatment of shock? 2. Which criteria can be considered most significant in the estimation of the depth of shock? The adequacy of a fluid in the treatment of shock must depend primarily on its ability to produce and maintain an increased volume of blood. Judged by this standard, blood is the most effective fluid available. The beneficial results obtained by the use of a 6 per cent solution of acacia (Bayliss¹²) led to its wide adoption as a therapeutic measure in cases of shock. Solution of acacia itself is incapable of transporting oxygen, but in view of the fact that in shock there is relatively little diminution of the oxygen-carrying erythrocytes in the blood stream and that concentration of the red blood cells almost invariably occurs, the use of this drug in the treatment of shock rests on a reasonable basis. Hypertonic solution of acacia and dextrose solution have been advocated

9. Freeman, N. E.: Decrease in Blood Volume After Prolonged Hyperactivity of Sympathetic Nervous System, *Am. J. Physiol.* **103**:185, 1933.

10. Malcolm, J. D.: The Nature and Treatment of Surgical Shock, *Tr. Med. Soc. London* **32**:274, 1909.

11. Gesell, R.: Studies on Submaxillary Gland: I. Dependence of Tissue Activity upon Volume-Flow of Blood and on Mechanism Controlling This Volume-Flow of Blood, *Am. J. Physiol.* **54**:166, 1920.

12. Bayliss, W. M.: Intravenous Injection in Wound Shock, London, Longmans, Green & Co., 1919.

(Erlanger and Gasser¹³), but the danger of acute cardiac dilatation after their administration has prevented their general use. The ready availability of isotonic solutions of sodium chloride and dextrose solutions has made them the commonly used fluids in the treatment of shock and hemorrhage. During an investigation on the metabolic effects of water, a peculiar abnormal response was noticed in animals which had been subjected to hemorrhage (Davis¹⁴).

This investigation was undertaken to determine the nature and mechanism of the response of normal animals and of animals in shock to water and electrolytes. The question was raised regarding the criteria of shock to be used in this study. In view of the fact that the central phenomenon of shock is an anoxemia which is the resultant of such factors as oligemia, lowered blood pressure, diminished volume flow of blood and peripheral vasoconstriction, it was decided that the rate of oxygen consumption of the animal provided a more accurate picture of the effects of traumatic shock on the tissues. However, determinations of the blood pressure level were made to serve as controls.

METHODS

Healthy dogs weighing from 10 to 20 Kg. were used throughout these experiments. Anesthesia was induced by sodium barbital in a dosage of 250 mg. per kilogram of body weight. Surgical anesthesia was essential in order to prevent movements which might falsify the metabolism readings. The metabolic rates of several unanesthetized animals, which had been trained for such determinations, were obtained. Sodium barbital was thereafter administered in the aforementioned dosage, and only a slight depression of the rate of oxygen consumption was noticed. Moreover, the metabolism readings of trained unanesthetized animals often showed variations of from 100 to 300 cc. of oxygen consumption per ten minutes. Especially was this noticeable when readings were obtained frequently and over long periods of time. In the animals anesthetized with sodium barbital, the rate of metabolism remained remarkably constant. The metabolism determinations were made with a Krogh respiratory apparatus before and at frequent intervals during each experiment. Prior to each experiment the urinary bladder was emptied by means of a catheter, which was left in situ, in order that the urinary secretion might be measured. Fluid was administered in the form of an isotonic solution of sodium chloride (0.9 per cent) heated to 38 C. This was permitted to run into the exposed femoral vein at a constant rate of 16 cc. per minute until 3,000 cc. was given, at which point the injection was stopped. A control series of twenty normal dogs was used. In another series of fifteen animals secondary shock was produced by (1) massive hemorrhage to the extent of one third of the calculated volume of blood, (2) repeated trauma to a hindlimb, (3) ligation of the portal vein and (4) the injection of histamine dihydrochloride.

13. Erlanger, J., and Gasser, H. S.: Hypertonic Gum Acacia and Glucose in the Treatment of Secondary Traumatic Shock, *Ann. Surg.* **69**:389, 1919.

14. Davis, H. A.: The Relation of Water and Electrolytes to Metabolism, *Science* **81**:493, 1935.

The blood pressure was recorded in the usual manner in the majority of these experiments.

Death following ligation of the portal vein has been ascribed to shock resulting from loss of blood and plasma into the wall of the bowel (Elman and Cole¹⁵). In this investigation it has been found that the onset of shock after obstruction of the portal vein may be appreciably hastened by the intravenous injection of an isotonic saline solution. Postmortem examination of these animals revealed an intense edema of the walls of the large and small intestines. The spleen was enlarged to as much as three times its normal size.

FLUIDS AND METABOLISM

The metabolic effects of water have been investigated both in human beings and in experimental animals, and it has been shown that the administration of water increases the rate of metabolism (Eichhorst,¹⁶ Feder,¹⁷ Falck and Falck,¹⁸ Genth,¹⁹ Gruzdiev,²⁰ Matzkevich,²¹ Becker,²² Neumann,²³ Panum,²⁴ Schöndorff²⁵ and Weigelin.²⁶ However, the most direct evidence that an increased intake of fluid augments cellular activity was provided by Hawk and his co-workers,²⁷ when they demonstrated

15. Elman, R., and Cole, W. H.: Hemorrhage and Shock as Causes of Death Following Acute Portal Obstruction, *Arch. Surg.* **28**:1166 (June) 1934.

16. Eichhorst, H.: Ueber die Resorption der Albuminate im Dickdarm, *Arch. f. Physiol.* **4**:570, 1871.

17. Feder, L.: Der zeitliche Ablauf der Zersetzung im Thierkörper, *Ztschr. f. Biol.* **17**:531, 1881.

18. Falck, E. P., and Falck, F. A.: Physiologische Studien über die Ausleerungen des auf absolute Carenz gesetzten Hundes, *Beitr. z. Physiol., Hyg. u. Toxicol.* **1**:1, 1875.

19. Genth, E. A.: Untersuchungen über den Einfluss des Wassertrinkens auf den Stoffwechsel, Wiesbaden, Kreidel & Niedner, 1856.

20. Gruzdiev, V. S.: Comparative Influence of Copious or Moderate Drinking of Water on Change of Matter, *Vrach* **11**:213, 1890.

21. Matzkevich, V. G.: Influence of Abundant Water Drinking on Assimilation of Nitrogenous Particles of Food, and Nitrogenous Metabolism in Typhoid Patients, St. Petersburg, P. Voshtshinskaya, 1890.

22. Becker, N. M.: De l'influence des solutions de bicarbonate de soude, de sel marin, d'acide carbonique et de quelques eaux alcalines sur la sécrétion du suc pancréatique, *Arch. d. sc. biol.* **2**:433, 1893.

23. Neumann, R. O.: Die Bedeutung des Alkohols als Nahrungsmittel, *Arch. f. Hyg.* **36**:1, 1899.

24. Panum, P. L.: Om urinstof—og urinsekretionens kurve efter en enkel maaltid om dagen, bestaaende af kød med eller uden tilsaetning af fedt, borsyre, rugbrød og vand, *Nord. med. ark.* **6**:1, 1874.

25. Schöndorff, B.: Ueber den Einfluss des Wassertrinkens auf die Ausscheidung der Harnsäure, *Arch. f. Physiol.* **46**:601, 1890.

26. Weigelin, J.: Versuche über die Harnstoffausscheidung während und nach Muskelthätigkeit, *Arch. f. Anat. u. Physiol.* **3**:207, 1868.

27. Howe, P. E.; Mattill, H. A., and Hawk, P. B.: The Influence of an Excessive Water Ingestion on a Dog After a Prolonged Fast, *J. Biol. Chem.* **10**:417, 1911-1912.

an increased excretion of total purine and nitrogen after the administration of fluid. The stimulating effect of water on metabolism which was demonstrated by these earlier workers was fully corroborated by subsequent investigators (Jarisch and Liljestrand,²⁸ Carpenter and Fox,²⁹ Rubner,³⁰ Barcroft,³¹ Zuntz,³² Verzár,³³ Tangl,³⁴ Janssen and Rein,³⁵ Lublin³⁶ and Grollman³⁷). The degree of stimulation produced by water is largely dependent on the mode of administration. When fluid is given subcutaneously, the rise in metabolism may be absent completely. A somewhat greater response results from the oral administration of water, and it has been pointed out that the ingestion of 500 cc. of water may increase the metabolic rate in man as much as 16 per cent above the initial level (Benedict and Carpenter³⁸). The intravenous ingestion of fluid causes a considerable rise in the rate of oxygen consumption. In the initial control experiments the following solutions were used: 0.9 per cent solution of sodium chloride, 5 per cent solution of dextrose and 10 per cent solution of sucrose. In each case a rise in metabolism occurred, the highest rates being encountered when dextrose solution was administered. In some instances the metabolic rate was increased by 200 to 300 per cent when dextrose solution was given, but the rise was not sustained and soon returned to the original level. Saline and sucrose solutions did not produce such great augmentations of the metabolism, which varied from 25 to 50 per cent, but the increase was longer sustained.

28. Jarisch, A., and Liljestrand, G.: Ueber das Verhalten des Kreislaufes bei Muskularbeit nach dem Essen und bei Flüssigkeitszufuhr, *Skandinav. Arch. f. Physiol.* **51**:235, 1927.

29. Carpenter, T. M., and Fox, E. L.: The Gaseous Exchange of the Human Subject as Affected by Ingestion of Water at 37° C., *J. Nutrition* **2**:359, 1930.

30. Rubner, M.: Die Gesetze des Energieverbrauchs bei der Ernährung, Leipzig, F. Deuticke, 1902.

31. Barcroft, J.: Zur Lehre vom Blutgaswechsel in den verschiedenen Organen, *Ergebn. d. Physiol.* **7**:744, 1908.

32. Zuntz, N.: Verdauungsarbeit und spezifisch-dynamische Wirkung der Nahrungsmittel, *Med. Klin.* **6**:351, 1910.

33. Verzár, F.: Die Wirkung intravenöser Kochsalzinfusionen auf den respiratorischen Gaswechsel, *Biochem. Ztschr.* **34**:41, 1911.

34. Tangl, F.: Colorimetrie der Nierenarbeit, *Biochem. Ztschr.* **53**:36, 1913.

35. Janssen, F., and Rein, H.: Ueber die Zirkulation und Wärmebildung in der Niere, *Klin. Wchnschr.* **6**:1827 (Sept. 17) 1927.

36. Lublin, A.: Ueber den Einfluss der Nierenarbeit auf den Gaswechsel des Menschen, *Ztschr. f. klin. Med.* **109**:371, 1929.

37. Grollman, A.: Physiological Variations in Cardiac Output of Man: Changes in Cardiac Output, Metabolism, Blood Pressure, and Pulse Rate of Man Following the Ingestion of Fluids, *Am. J. Physiol.* **89**:157, 1929.

38. Benedict, F. G., and Carpenter, T. M.: Food Ingestion and Energy Transformations with Special Reference to the Stimulating Effect of Nutrients, Publication 261, Carnegie Institution of Washington, 1918, p. 355.

METABOLIC RESPONSE TO INJURY

Before further consideration is given to the effects of the administration of fluid in cases of shock, a brief review of the alterations in metabolism in cases of secondary shock might be presented. Secondary or traumatic shock is accompanied by a fall in the rate of oxygen consumption (Aub³⁹ and Henderson and co-workers⁴⁰). In this investigation diminutions of from 30 to 50 per cent of the original rate were commonly noticed. It was found that the extent of the fall of the metabolism seemed to be dependent on the mode of production of shock (Davis¹⁴). Shock resulting from a single large hemorrhage is charac-

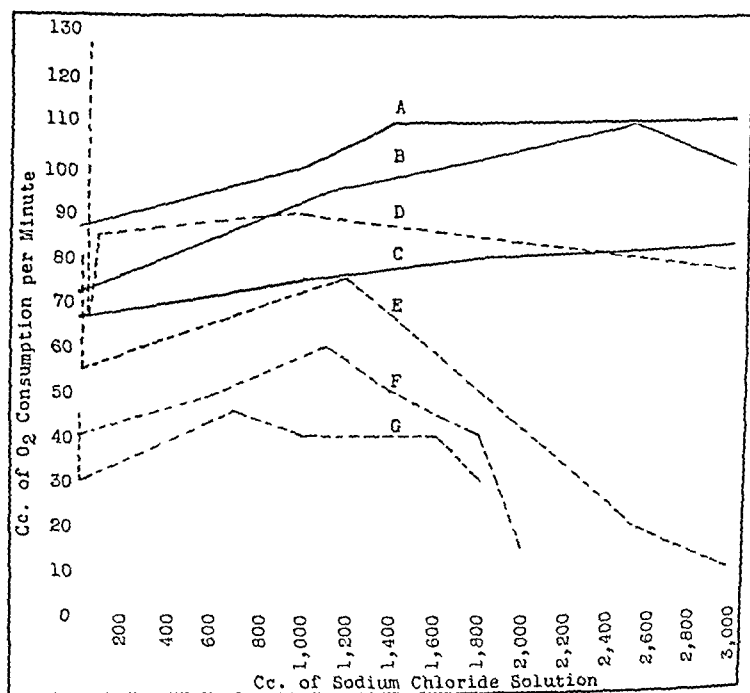


Fig. 1.—Curves showing the influence of the administration of water on the rate of oxygen consumption in normal animals and in animals in shock. *A*, *B* and *C* are the curves for the normal control animals; *D*, the curve for an animal in which shock was produced by extensive hemorrhage; *E*, the curve for an animal in which shock was produced by trauma plus hemorrhage, and *F*, the curve for an animal in which shock was produced by obstruction of the portal vein.

terized by a tendency to rapid and spontaneous recovery. When severe trauma is involved, the metabolic rate has a tendency to remain fixed at a low level, and the return to normal is considerably delayed. Immediately after ligation of the portal vein, the rate of oxygen consumption

39. Aub, J. C.: Studies in Experimental Traumatic Shock: I. Basal Metabolism, *Am. J. Physiol.* **54**:388, 1920.

40. Henderson, Y.; Prince, A. L., and Haggard, H. W.: Observations on Surgical Shock, *J. A. M. A.* **69**:965 (Sept. 22) 1917.

is unaffected, sometimes for an hour or more. Thereafter, a progressive downward tendency may be noted, with death as the end-result. The influence of histamine dihydrochloride is variable. Usually a fall in metabolism occurs, which in the experiments reported here has not been great. The decrease in metabolism, however, tends to be maintained for a long period. While these are the primary metabolic phenomena associated with shock, certain later changes must be taken into consideration. Within twenty-four hours an increased nitrogenous output in the urine occurs, and this is associated with a rise in metabolism (Cuthbertson⁴¹), which continues for periods varying from seven to ten

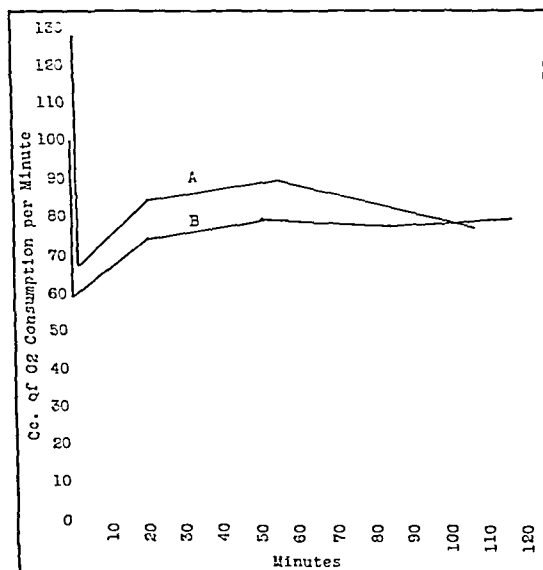


Fig. 2.—Curves showing the metabolism readings of animals which recovered spontaneously from hemorrhage. *A* is the curve of an animal that received saline solution, and *B*, the curve of an animal that did not receive saline solution.

days. This excretion of sulfur creatinine and potassium has been explained by the autolysis of injured tissues at the site of trauma.

ANOXEMIC EFFECTS OF FLUID IN SHOCK

It has been stated already that the metabolic rate of normal animals is increased by the intravenous injection of fluid. The maximal increase varies between 25 and 50 per cent and is reached only after from 1,400 to 2,400 cc. of fluid has been given. Thereafter, a plateau is obtained in the curve, and this is maintained so long as the fluid is

41. Cuthbertson, D. P.: Observations on Disturbance of Metabolism Produced by Injury to Limbs, *Quart. J. Med.* 1:233, 1932.

injected and for some time afterward. Generally, the absolute increase in the rate of oxygen consumption varies directly with the initial rate of metabolism. In a normal healthy animal the tolerance for water is great. Fluid to the extent of 25 per cent of the total body weight of the animal may be given without any deleterious result.

In traumatic shock a peculiar alteration of the metabolic response to fluids takes place. The maximal increase in the rate of oxygen usage is reached at an earlier stage during the injection of fluid, i. e., after from 700 to 1,200 cc. of the solution has been given. Thereafter, if more fluid is given, a progressive decline in the rate of oxygen consumption takes place. Apparently in shock tolerance for fluids is much diminished, as the administration of a quantity of water equivalent to only from

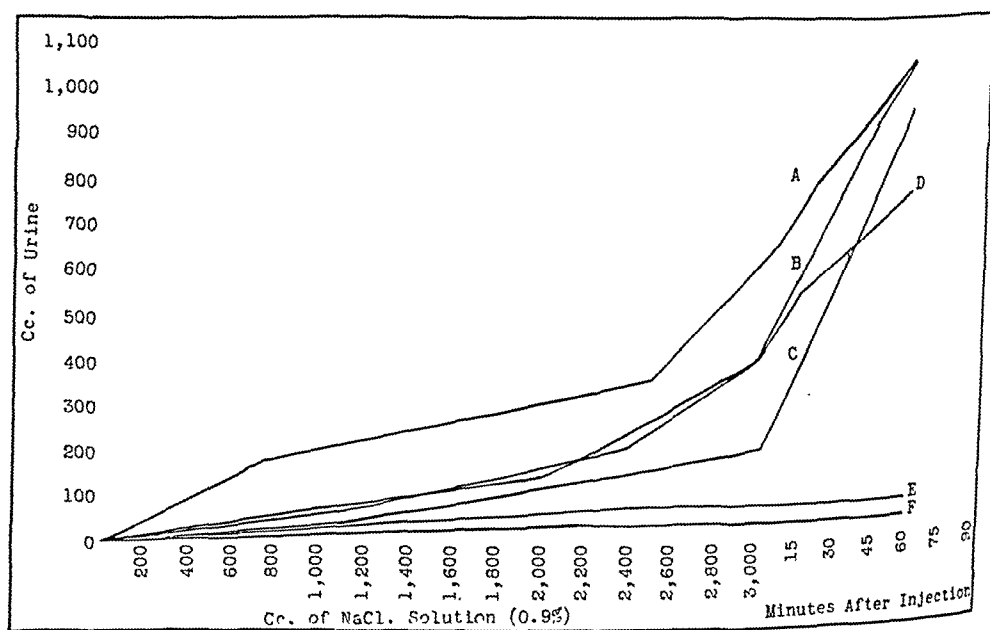


Fig. 3.—Curves showing the urinary secretion of animals in shock in relation to the administration of fluids. *A*, *B* and *C* are the curves of normal control animals. *D* is the curve of an animal in which shock was produced by the injection of histamine dihydrochloride; *E*, the curve of an animal in which shock was produced by hemorrhage, and *F*, the curve of an animal in which shock was produced by trauma.

5 to 12 per cent of the body weight produces a fall in the metabolic rate. In this investigation it was noted that the degree of intolerance for fluids varied with the depth of shock induced. It was particularly noticeable in those animals exposed to severe trauma. Hemorrhage in small amounts did not alter the metabolic response, as such animals reacted in almost a normal manner. Shock produced by ligation of the portal vein invariably diminished the tolerance of the animal for fluid.

The reason for the diminished tolerance for water of the animal in shock is difficult to state. Certainly, previous investigations point to

the fact that the stimulant action of fluids on the metabolism is greatest while the fluid is in the blood vessels, and therefore can be attributed to an increase in the blood volume, rate of blood flow or both (Davis⁴²). In shock, the fluid leaves the vascular bed rapidly, in spite of the existing concentration of the blood. This explains the ephemeral nature of the stimulant action of water on the rate of oxygen consumption, but it does not explain the depressant action of water in traumatic shock.

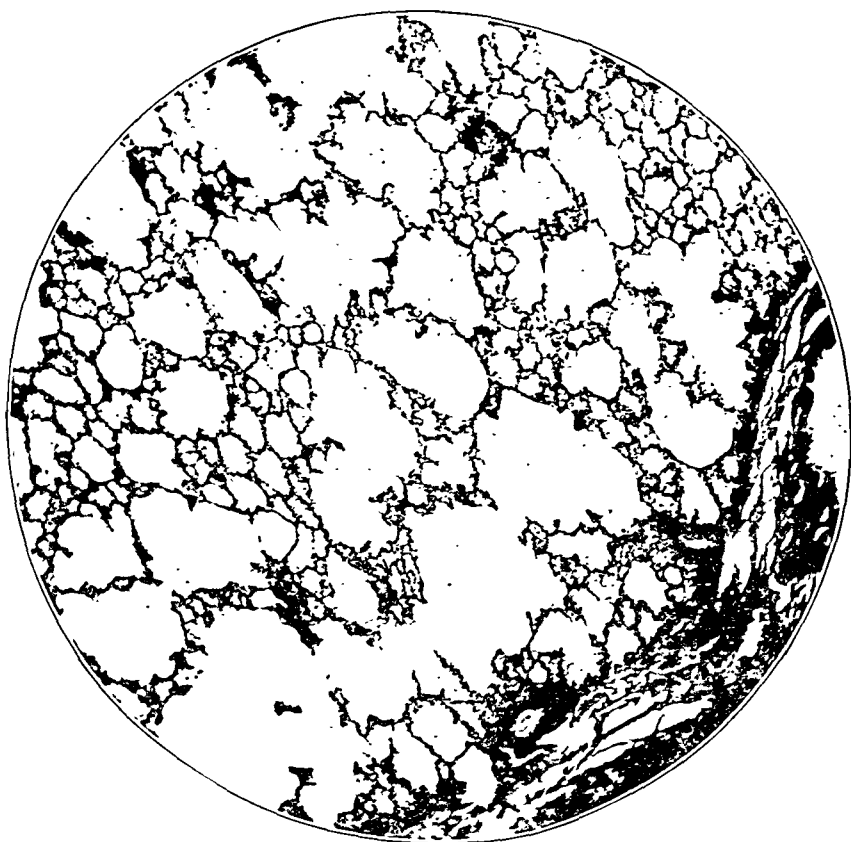


Fig. 4.—Photomicrograph of a section of the lung of an animal in which shock was produced by trauma; $\times 50$. Acute congestion of the alveolar capillaries and minimal alveolar edema are evident.

Anoxemia, which is already present in shock, is intensified with amounts of fluid which would not affect a normal animal. In some way the transport, transfer or utilization of oxygen is affected.

42. Davis, H. A.: Studies in Water Balance: I. Excessive Oxygen Usage Response of Dehydrated Animals to Water and Electrolytes, *Proc. Soc. Exper. Biol. & Med.* **33**:242, 1935.

RENAL FUNCTION IN SHOCK

In secondary shock not only is there an alteration in the metabolic response, but there is also a change in the renal function. The injection of a 0.9 per cent solution of sodium chloride into a normal animal was followed by a brisk diuresis, which commenced shortly after the initiation of the injection. Within one hour after completion of the infusion,

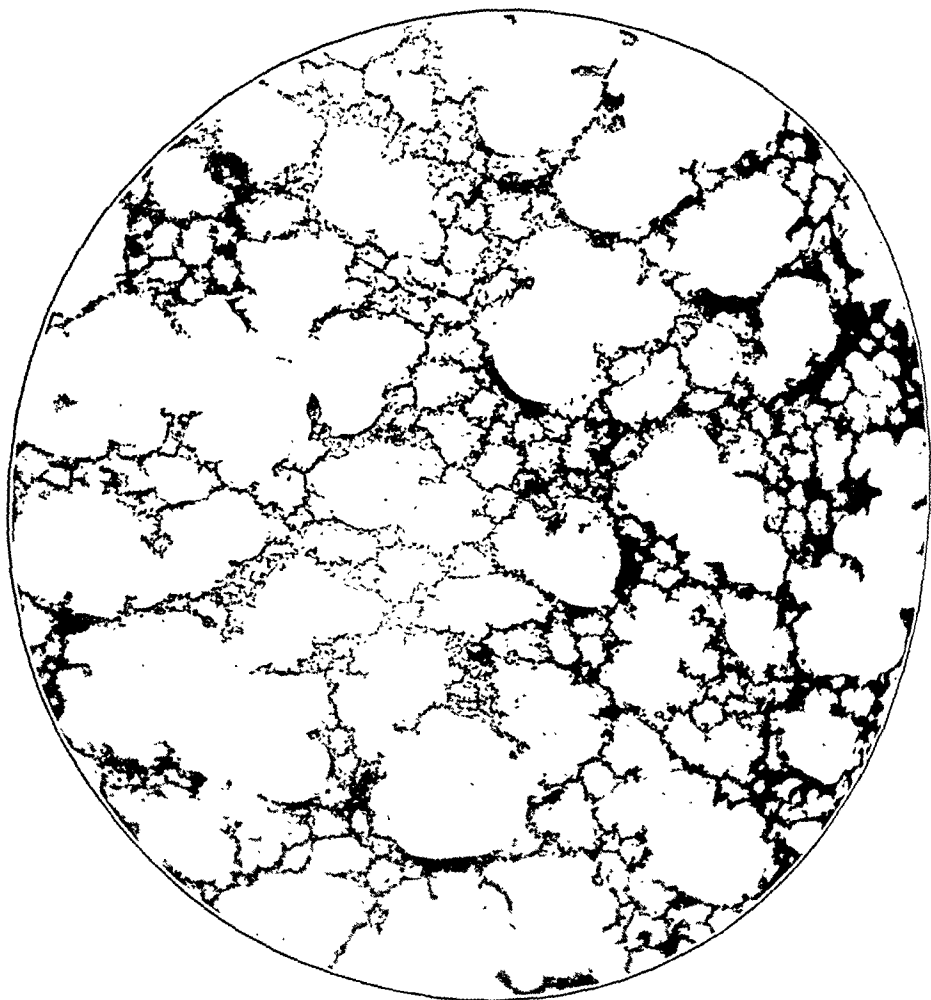


Fig. 5.—Photomicrograph of a section of a lung of an animal with traumatic shock which was treated by the administration of fluids; $\times 50$. Acute congestion of the alveolar capillaries and moderate alveolar edema are evident.

the urinary secretion was abundant, and volumes equivalent to one third or one half of the total amount of fluid given were obtained. In secondary shock, water diuresis is minimal, even after the infusion of large amounts of fluid. The extent of the water diuresis varies inversely with the depth of shock present.

While acidosis favors the release of water from tissues (Davis and Dragstedt⁴³), its presence in association with traumatic shock is of little value. This traumatic anuria is probably related to the lowering of the filtration pressure within the glomerular capillaries. Histologic studies of kidneys removed from animals in which shock had been produced reveal the presence of an acute cloudy swelling of the tubular

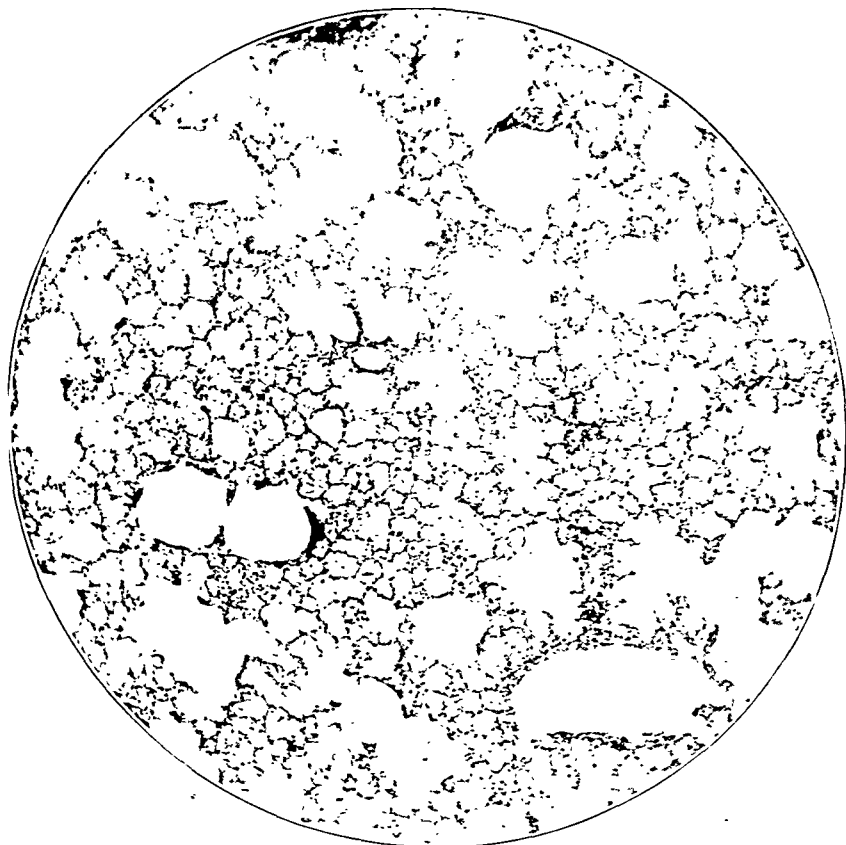


Fig. 6.—Photomicrograph of a section of the lung of a normal animal treated with fluids; $\times 50$. No congestion of the alveolar capillaries is evident, but extensive alveolar edema may be seen.

epithelium with pyknosis of nuclei. The glomerular capillaries are greatly congested, but no specific lesions are demonstrable. These alterations in the tissues are reversible, and no permanent renal injury

43. Davis, H. A., and Dragstedt, L. R.: The Relative Significance of Electrolyte Concentration and Tissue Reaction in Water Metabolism. *Am. J. Physiol.* **113**:193, 1935.

occurs. However, the presence of anuria is significant, as it emphasizes the inability of the organism in shock to distribute freely within itself ingested fluids.

NATURE OF THE ANOXEMIC RESPONSE

The exact mechanism of production of the anoxemia resulting from the administration of fluids in cases of secondary shock is debatable.

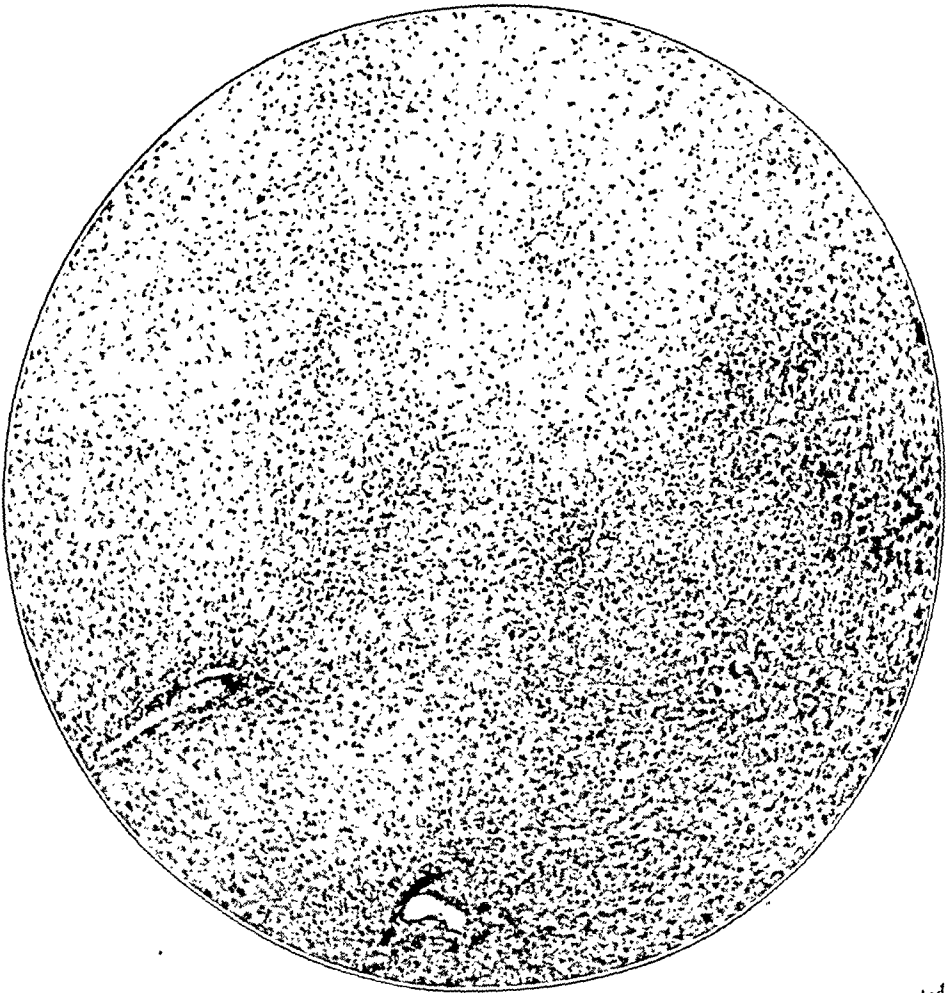


Fig. 7.—Photomicrograph of a section of the liver of a normal animal treated with fluids; $\times 50$. Intense edema of the liver cells, with compression of the liver capillaries, and clear nuclei without pyknosis are evident.

A diminution of oxygen usage might result from (1) an insufficiency of oxygen available to the blood in its passage through the lungs, (2) a decrease of available oxygen-carrying material and (3) interference with oxygen utilization by the cells. The third cause may, with justification, be excluded in view of the fact that the administration of large quantities of fluids sufficient to produce obvious generalized edema of

the tissues in normal animals causes no decrease in the rate of oxygen consumption. It is possible, however, that in shock the utilization of oxygen by anoxic tissues may be diminished by the presence of large amounts of inert fluid.

Attention was focused on the first two of these possible causes. Two subsidiary investigations were therefore undertaken. In order to examine the factor of pulmonary changes in the production of anoxemia

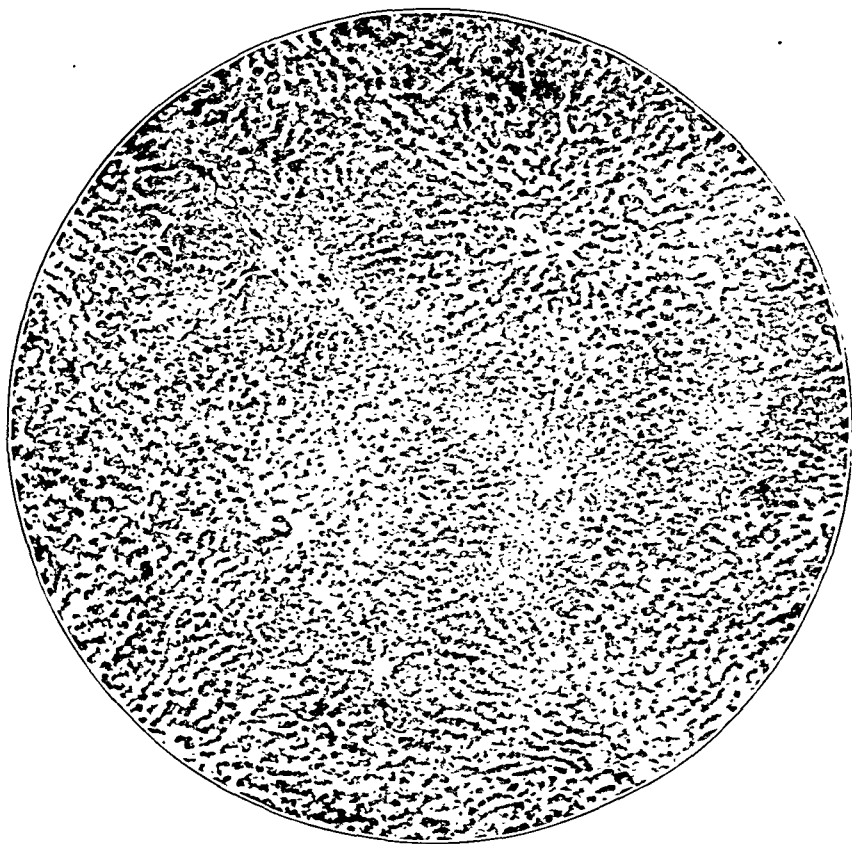


Fig. 8.—Photomicrograph of a section of the liver of an animal with traumatic shock which was treated by the administration of fluids; $\times 50$. Acute congestion of the central capillaries with compression of the liver cells and slight nuclear pyknosis at the periphery of the nodules are evident.

resulting from shock with and without the administration of fluids, the following experiment was designed:

A series of healthy dogs weighing from 8 to 20 Kg. was used. Pentobarbital sodium was used in a dosage of 0.03 Gm. per kilogram of body weight. Shock was induced (1) by repeated trauma to both hindlimbs and (2) by repeated

hemorrhage. Kymographic tracings of the blood pressure were made. When the blood pressure was lowered to 60 mm. of mercury or less, the animal was considered to be in shock. Usually the blood pressure was maintained in the neighborhood of from 40 to 50 mm. of mercury. In order to obviate any pulmonary changes due to prolonged immobilization, the period of shock was not permitted to exceed one and one-half to two and one-half hours. Each animal was moved into various positions during the experiments. Each animal was killed either by intensification of the shock present or by air embolism, and the lungs and other viscera were immediately removed and placed in a hot diluted solution of formaldehyde U. S. P. (1:10). Four groups of experimental animals were studied: group a, animals given pentobarbital; group b, normal animals that received fluid; group c, animals in shock, and group d, animals in shock that were given fluids.

Histologic changes were absent in the lungs of the animals of group a. In the animals in group b edema was present in the alveolar spaces. This was not uniform in distribution, however, and little or no cellular reaction was observed. The histopathologic picture found in the animals of group c will be described in a forthcoming paper. The findings pertinent to the discussion here will be described. In animals in shock edema was present in scattered areas throughout both lungs. But it was not great in amount and was less than that found in the lungs of normal animals receiving fluids. In the animals of group d edema was not conspicuous and was less than that present in the animals of group b.

These findings provide no basis for the assumption that the anoxemia of shock results from pulmonary edema. Moreover, edema of the lungs does not seem to be a significant factor in the production of the anoxemia following the injection of fluids into the animal in shock.

Changes in the tissues resulting from the administration of fluids depend primarily on the state of the vascular bed. When fluids enter the circulatory system in amounts sufficient to increase the volume of circulating blood, adaptation mechanisms are at once brought into play. In table 1 are described briefly certain visceral changes accompanying the administration of fluid to normal animals and to animals in shock.

This brief summary of the visceral changes in animals in shock which received fluid and in those which did not receive fluids reveals a paradoxical phenomenon. In the animals with traumatic shock, a condition in which capillary permeability is increased, the administration of fluid produced less pulmonary edema than in the normal animals. This paradox is readily explainable by the fact that in shock much of the fluid escapes from the circulatory system at the point of least resistance—the area of trauma. It was noted in these animals that the traumatized limbs became very edematous, which would be consistent with the finding of only mild pulmonary edema, relatively little peri-

toneal transudate and the histologic evidence of water storage localized to the central portion of the hepatic lobules.

The final part of this investigation was undertaken to determine to what extent the use of fluid could produce a loss of protein and cellular elements from the blood of normal animals and of animals in shock. Standard amounts of fluid (60 cc. per pound of body weight) were given to the animals by vein, and the peritoneal transudate was

TABLE 1.—*Tissue Changes Resulting From Administration of Fluid in Normal and Traumatized Animals*

Viscera	Normal Animal; Fluid Administered	Animal in Shock	Animal in Shock; Fluid Administered
Lung	Considerable general edema fluid in alveoli; no capillary congestion; no cellular reaction in alveoli; no petechial hemorrhage	Mild discrete patchy distribution of edema in alveoli; marked cellular reaction with mononuclear and polymorphonuclear cells; acute congestion of alveolar capillaries with diapedesis of red blood cells; areas of hemorrhage and petechiae	Mild edema of alveoli with considerable cellular reaction—monocytes and polymorphonuclears; acute congestion of alveolar capillaries with diapedesis of red blood cells; areas of hemorrhage in alveoli; subpleural petechiae
Kidney	Slight increase in size; distention of Bowman's capsule; no glomerular lesions; tubular epithelium normal with large vesicular nuclei and well defined chromatin material	Slight diminution in size; acute cloudy swelling of tubular epithelium with small pyknotic nuclei; congestion of glomerular capillaries	Early cloudy degeneration of tubular epithelium with small pyknotic nuclei; no glomerular lesions
Liver	Larger than normal; marked edema and vacuolization of liver cells; nuclei large, clear and vesicular, with well defined chromatin material; moderate capillary dilatation in region of central vein	Slightly larger; marked congestion of liver capillaries in region of central vein; liver cells small, compressed with small pyknotic nuclei	Slightly larger; mild edema and vacuolization of hepatic cells around central vein where nuclei are large and vesicular; cells stain deeply with small pyknotic nuclei in periphery of lobule
Spleen	Enlarged; edema of splenic pulp spaces; dilatation of splenic sinusoids	Small; congestion of splenic sinusoids	Small; congestion of splenic sinusoids
Heart	Moderate dilatation—right auricle and ventricle; no histopathologic changes	Contracted; no histopathologic changes	Moderate dilatation; no histopathologic changes
Pancreas	No specific pathologic process	No specific pathologic process	No specific pathologic process

carefully measured and examined for total proteins, albumin and globulin and for erythrocytes after centrifugation.

The representative data, shown in table 2, suggest that in the intact animal the administration of fluid leads to a loss of albumin and globulin from the blood stream. The loss of protein into the peritoneal fluid is 9.5 per cent (calculated on the basis of a blood serum content of 7 Gm. per hundred cubic centimeters of blood). The percentage of protein lost in the animal in shock that is treated with fluid is equal to, and probably greater than, that found in the intact animal. It will be

noted that in dogs 3 and 4 the percentage calculations have been made on the basis of normal calculated volumes of blood. As the volume of blood is reduced in traumatic shock, the percentage of protein lost in animal 3 is probably higher than is shown by table 2.

COMMENT

This study seems to indicate the presence of certain physiologic and pathologic limitations to the free and equal distribution of fluids in the organism in shock. The introduction of fluid into the intact animal produces a dilution of the blood with subsequent diuresis. With larger amounts of fluid, the liver cells imbibe water from the blood stream and become edematous, ultimately causing compression of the hepatic capillaries. Still later, the splenic sinusoids dilate. A transudate of protein-laden fluid occurs into the peritoneal cavity. Finally, the fluid containing serum albumin and globulin permeates through the capillary walls, par-

TABLE 2.—*Effect of Sodium Chloride Solution (0.9 Per Cent) on Protein Loss into Peritoneal Cavity*

Dog No.	Type of Experiment	Calculated Blood Volume, Cc.	Calculated Total Protein in Blood, Gm.	Peritoneal Fluid, Cc.	Peritoneal Fluid			Protein Loss, %
					Total Protein, Gm. per 100 Cc.	Albumin, Gm. per 100 Cc.	Globulin Gm. per 100 Cc.	
2	Control animal; fluid administered	738	51.0	250	4.67	3.78	1.09	9.5
3	Animal in shock; fluid administered	553	38.5	100	3.59	2.79	0.80	9.3
4	Animal in shock (traumatic)	1,353	94.5	10	5.70	4.20	1.50	0.6

ticularly those of the lungs, leading to pulmonary edema. In secondary shock the normal reservoir action of the blood for fluids is lost, and fluid leaves the blood stream more rapidly than in the intact animal (Davis⁴⁴). The site of fluid loss is greatest in the region of trauma, so that relatively little transudation of fluid occurs into the peritoneum or into the alveoli of the lungs. Evidences of water imbibition are present in the central portions of the hepatic lobules. It cannot be stated definitely here whether or not this localization of water storage by the liver is indicative of inability of the liver cells to store water or of an insufficient quantity of water available for storage. The production of a lowered rate of oxygen consumption by the administration of fluids in cases of secondary shock does not result from interference with the supply of available oxygen by pulmonary edema. The stimulant action of water on metabolism is exerted only so long as fluid is actually present

44. Davis, H. A.: The Behaviour of Isotonic and Hypertonic Solutions in the Blood Stream of Normal and Dehydrated Animals, *Proc. Soc. Exper. Biol. & Med.* **32**:210, 1934.

within the circulatory system and seems to depend on the resultant increase of blood volume or blood flow (Davis⁴²). Removal of serum albumin and globulin and of blood cells by the introduced fluid into the area of trauma and peritoneal cavity diminishes the material available for transportation of oxygen and leads to a still greater degree of oxygen want.

CONCLUSION

In traumatic shock a peculiar alteration of the response to fluids exists. The physiologic availability of water is diminished even to the point of actual intolerance (Davis⁴⁵). Even the transfusion of blood, as has been pointed out by Zunz and Govaerts,⁴⁶ can be harmful. The administration of a quantity of fluid equivalent to from 5 to 12 per cent of the body weight may result in a fall in the metabolic rate. The intact animal, on the contrary, may be given fluid to the extent of 25 per cent of the total body weight without any diminution in the rate of oxygen consumption. The anoxemia of traumatic shock is augmented by the administration of fluids, which promote a loss of protein and cells into the traumatized area, into the peritoneal cavity and, to a slight extent, into the alveoli of the lungs and general tissue spaces.

45. Davis, H. A.: Influence of Water Administration upon Oxygen Consumption Rate in Shock, *Proc. Soc. Exper. Biol. & Med.* **34**:21, 1936.

46. Zunz, E., and Govaerts, P.: Recherches expérimentales sur les effets de la transfusion dans les divers états de collapsus circulatoire, *Bull. Acad. roy. de méd. de Belgique* **29**:796, 1919.

EXTENSIVE BURNS

TREATMENT WITH SILVER NITRATE AND METHYL ROSANILINE

HIRA E. BRANCH, M.D.

DETROIT

The ideal treatment for burns is one that, first, saves the patient's life; second, eliminates pain, shock and toxemia; third, reduces the morbidity to a minimum, and fourth, allows the burned area to heal quickly without skin grafting being necessary.

The method of treating burns to be brought out in this paper approaches closely to the "ideal" treatment, as may be seen by the accompanying table. First, there have been no deaths in cases in which the treatment has been used thus far, and there were only seven deaths in ninety-five cases in which this form of therapy was used during its development. Second, the period of pain and shock was very short. Toxemia did not develop as a serious threat. Third, the morbidity was greatly reduced, for the patients were turned about in a few hours and were urged to get up and about in a few days and to wait on and amuse themselves. Fourth, skin grafting was done in only one case. However, the mere use of this combination treatment for the local area did not do all the aforementioned things alone; naturally measures for the general upbuilding of the patient were also carried out.

BRIEF RÉSUMÉ OF MODERN TREATMENTS FOR BURNS

In 1925 the late Dr. Edward C. Davidson¹ published his famous paper entitled "Tannic Acid in the Treatment of Burns," in which the use of compresses on the injured areas was advised, a 2.5 per cent aqueous solution of tannic acid being employed. Attempts to make a satisfactory ointment of tannic acid at that time failed, chiefly because an oily base was used. Later, a spray of a 5 per cent aqueous solution of tannic acid was used in place of the compresses. There is now little question but that the spray did revolutionize the manner of dealing with burns. The mortality rate has been lowered from 35 or 38 per cent to 10.5 or 12 per cent. Later, this treatment was altered somewhat by the use of a 5 per cent tannic acid gel, a mixture of tannic acid in a water-

The experimental work for this monograph was done at the Children's Hospital of Michigan, while the author was in the surgical service.

1. Davidson, E. C.: Tannic Acid in the Treatment of Burns, Surg., Gynec. & Obst. 41:202-221 (Aug.) 1925.

soluble base. The principles of treatment are the same with the gel as with the solution, but the tanning process is much slower with the former.

There were little or no changes of note in the management of burns from 1925 till 1932, as far as the treatment of the local area was concerned. Big strides were made in treating the general condition of the patient, the water balance and the chloride and plasma protein contents being carefully watched. However, this has been dealt with elsewhere. In 1932 Dr. Robert Henry Aldrich² read a paper in Boston on "The Role of Infection in Burns," which dealt with the theory and treatment of burns with special reference to methyl rosaniline (gentian violet). The mortality rate for burns treated with this drug dropped to the same level as that for burns treated with tannic acid, namely, from 10 to 12 per cent. The methyl rosaniline was sprayed on the burned area in the form of a 1 per cent aqueous solution. Again a gel was made, the methyl rosaniline being used in a water-soluble base. This gel has been used chiefly in the treatment of ambulatory patients with minor burns and is an excellent way of dealing with them. A generous coat of the gel is spread over the burn, and a bandage is applied which is not removed for about ten days. Practically all burns are cleanly healed in that time.

The next step forward was taken by Dr. A. G. Bettman³ in 1935, when he combined the use of a solution of silver nitrate over one spray of tannic acid, thus obtaining an immediate black crust over the injured surface. This saved about four hours in the tanning process. However, the disadvantages and the advantages of this method were the same after the first few hours as those of the tannic acid alone. Perhaps it is now advisable to list the advantages and disadvantages of the aforementioned treatments.

ADVANTAGES AND DISADVANTAGES OF VARIOUS METHODS OF TREATMENT

Tannic Acid.—Herewith are quoted some of Dr. Davidson's conclusions as to the advantages of treatment with tannic acid:

Coagulation of the devitalized tissue by the use of tannic acid lessens toxemia. Tannic acid as an initial dressing has an analgesic effect.

The subsequent use of the open air method causes minimal trauma and promotes general comfort.

2. Aldrich, R. H.: The Rôle of Infection in Burns, *New England J. Med.* **208**:299-309 (Feb. 9) 1933.

3. Bettman, A. G.: Tannic Acid-Silver Nitrate Treatment of Burns, *North-west Med.* **34**:46-51 (Feb.) 1935.

4. Davidson, E. C.: The Prevention of the Toxemia of Burns: Treatment by Tannic Acid Solution, *Am. J. Surg.* **40**:114-115 (May) 1926. Davidson.¹

The local astringent effect prevents the loss of body fluid.

Secondary infection is limited by this method of treatment because of the absence of a favorable nidus for bacterial growth.

Scar tissue formation has been lessened.

The protective layer of coagulated protein forms a scaffold for the growth of the young epithelial cells over the denuded surface.

The tannic acid treatment has brought a decided drop in the mortality rate for burns.

A uniform method of dealing with burns has been established throughout the world.

Some of the disadvantages of the treatment with tannic acid are:

1. The patient must remain quiet while covered with the black coagulum, otherwise cracking occurs. This stationary position favors pneumonia and aural infections and does not promote the "will to live" spirit so often needed by the patient with an extensive burn.

2. Cracking of the coagulum brings about infection, which usually requires removal of the crust.

3. The coagulum sticks tenaciously to the third degree areas of the burn, requiring surgical removal. (The soaking of a tannic acid crust is contraindicated because of infection and toxemia.)

4. Surgical removal of the black coagulum destroys many islands of epithelium beneath, which invariably necessitates skin grafting to the denuded areas.

Methyl Rosaniline Spray.—The advantages of using a spray of methyl rosaniline solution are the same as for tannic acid, with the following differences:

1. The crust that forms is pliable, but if it should crack the area is merely resprayed and infection is limited.

2. Infection is prevented, and if it is present before treatment is started methyl rosaniline helps to eradicate it.

3. Débridement of the burn does not have to be as severe.

4. The crust formed by methyl rosaniline can be soaked off, thus preserving the epithelial islands beneath. This practically eliminates skin grafting.

The disadvantages of this type of treatment are:

1. The solution has no astringent effect and does not prevent loss of body fluids.

2. The crust takes from one to three days to form, owing to the fact that the devitalized proteins are not coagulated.

Silver Nitrate-Tannic Acid Treatment.—Except for the rapid tanning effect and the saving of a few hours in that respect, the advantages and the disadvantages of this combination of drugs are practically the same as those for tannic acid alone.

EVOLUTION OF THE SILVER NITRATE-METHYL ROSANILINE TREATMENT

The principles of the treatment of burns with tannic acid are sound. This has been proved by the late Dr. Davidson and others. Clear evidence has been shown by the decrease in mortality from about 35 per cent to about 10 or 12 per cent. However, the solution is contraindicated in infected areas or surfaces that bend or are subject to infection, such as the perineum, fingers, toes, scalp, etc. During 1935 I experimented with various combinations of treatments, always using tannic acid as the basic treatment, chiefly because of its beneficial qualities and also because Dr. Grover C. Penberthy, with the late Dr. Davidson, had thoroughly established that form of treatment at the Children's Hospital of Michigan, in Detroit, where this work was done.

The first combination tried was the use of a spray of a 5 per cent solution of tannic acid on all clean areas that did not require motion or were not subject to infection. A 1 per cent aqueous solution of methyl rosaniline was used on all areas that were either infected or likely to become infected. The results were a great improvement over those obtained with tannic acid alone. The next modification was the combination of silver nitrate with the tannic acid on the clean areas and methyl rosaniline on the potentially dirty surfaces. The results were about the same as with the first combination.

The disadvantages have all been listed previously. However, the main ones were that the patient had to remain quiet for from two to three weeks, sometimes with his extremities in slings off the bed. The crust formed by the tannic acid had to be removed surgically from the deeper burned areas, necessitating skin grafting. The methyl rosaniline did not form an immediate crust and stop the loss of body fluids. The next problems were to find a combination which not only would stop these abuses but would keep the mortality rate down, prevent pain, shock and toxemia, reduce the morbidity (absolute rest in bed chiefly), and lastly, allow the burned surfaces to heal quickly without skin grafting. The methyl rosaniline prevented infection and toxemia and reduced morbidity and the amount of skin grafting, but the pain, shock and loss of body fluids were not eliminated, and the mortality rate was still about 10 to 12 per cent. The crusts formed by the tannic acid prevented pain and toxemia if infection did not occur. However, the

morbidity and skin grafting were not lessened remained about the same. Methyl rosaniline acid to give any advantageous qualities. Silver merely formed a black crust immediately over the black crust was due partly to a precipitation of tannate and partly to a coagulation of the dev.

The next combination used was silver nitrate. The results were excellent. The 10 per cent solution acted on the proteins of the serum exuding from the burn immediately lay down a milky white coagulum in the place of tannic acid in coagulating the proteins and loss of body fluids. The methyl rosaniline stain was used and aided in destroying and preventing infection. In a period of three weeks that the second degree burns crust had cracked off. The third degree areas were covered by a violet coagulum, but this was easily removed by soaking and by the use of compresses. On soaking of the burn invariably enough epithelial islands beneath so that a graft was necessary. After the coat was off compresses soaked in silver chloride, 1:200 solution, or compresses or gauze soaked in silver chloride was used to stimulate epithelization of the denuded area. The period of pain and shock was practically eliminated. Septicemia rarely developed. The amount of pain relievers necessary was greatly reduced. The mortality decreased, for the patients could be freely turned and after the first few days they could be removed from the hospital and allowed to walk about. Their general spirits improved.

During 1935, the transition period from treatment by the old to the new silver nitrate-methyl rosaniline method, 10 patients were treated whose burns were severe enough to necessitate hospitalization. Of these, seven died, giving a mortality of 70 per cent. In 1936, through June, eighteen patients with burns severe enough to necessitate hospitalization were treated by the new silver nitrate-methyl rosaniline method. The results are presented in the accompanying table. There were no deaths; all the patients were out of the hospital about during their recovery, unless they were too weak to be moved. The period of hospitalization was very short. Only one patient required a skin-grafting operation. The highest temperature

Data on Burns Treated by Silver Nitrate and Methyl Rosaniline

Case	Sex	Color	Age	Age of Burn, Hrs.	Etiology	Previous Treatment	Degree of Burn	Extent of Body Surface, %	Location	Period of Complete Rest in Bed	Highest Temperature (R.)	Average Temperature (R.)	Skin Grafting	Results
1	M	W	2½	24	Fire	Olive oil	2-3	20	Head; neck; back	5 days	102.0	100.0	0	Recovery
2	M	W	1	4	Coffee	Oil	2-3	20	Chest; right thigh; abdomen; perineum	2 days	102.0	99.1	0	Recovery
3	M	W	1½	48	Water	Ointment	2	15	Buttocks; back; thighs	8 days	101.6	99.0	0	Recovery
4	M	W	8	24	Water	Ointment; oil	3	35	Head; neck; back; arms	6 days	102.0	100.0	1	Recovery
5	F	W	3½	48	Fire	None	2	12	Face; chest; left arm	1 day	101.6	99.8	0	Recovery
6	M	W	11	9	Coffee	Lard; ointment	2-3	15	Abdomen; perineum; thighs	5 days	102.4	100.0	0	Recovery
7	M	W	10 mo.	1	Water	None	3	18	Head; trunk; left arm	8 days	105.1	100.8	0	Recovery
8	F	W	9	1	Water	Ointment	2-3	10	Left side of body; arm; leg	1 day	101.1	99.8	0	Improvement
9	M	W	1	20	Coffee	Ointment	3	12	Chest; right arm	7 days	102.4	99.8	0	Recovery
10	M	W	2½	1	Water	None	2-3	30	Trunk; right arm; left leg	2 days	100.1	99.0	0	Improvement
11	M	W	7 mo.	11	Cleaning solution	Tannic acid gel	2-3	25	Trunk; thighs	1 day	101.8	100.6	0	Recovery
12	M	N	2	1	Water	None	2-3	25	Neck; trunk; arms	5 days	101.1	101.0	0	Recovery
13	F	W	8	2	Fire	None	2	8	Face; neck; chest	4 hours	101.2	99.0	0	Recovery
14	M	W	1	1	Water	Oil; ointment	3	35	Head; trunk; right arm	6 days	101.0	100.1	0	Recovery
15	M	N	7	1	Water	Oil	2	8	Head; neck; chest	2 days	102.6	99.1	0	Recovery
16	F	W	2	1	Water	Oil; tannic acid ointment	2-3	12	Back; perineum	1 day	100.2	99.0	0	Recovery
17	P	W	1	3	Water	Ointment	2	10	Arms; legs; chest	2 days	102.2	100.0	0	Improvement
18	M	W	1	2	Water	None	2	5	Left leg; perineum	3 days	100.6	97.6	0	Improvement

* Unless otherwise stated, the age is given in years.

ROUTINE TREATMENT WITH SILVER NITRATE-METHYL ROSANILINE

After the patient is burned, the following procedures are carried out:

1. A large dose of sedative is given—codeine or morphine sulfate with phenobarbital.

2. The burned areas are washed with tincture of soft soap.

3. Débridement of the burn is done lightly and rapidly by merely breaking the blisters and removing the loose skin. The area is then washed with a sterile saline solution or a solution of boric acid.

4. The burn is sprayed at once with a 1 per cent aqueous solution of methyl rosaniline, and after three or four minutes the entire burned area is swabbed with a 10 per cent solution of silver nitrate.

5. The patient is placed in a burn tent at a temperature of 85 to 90 C. The area is resprayed with a 1 per cent solution of methyl rosaniline every fifteen minutes for about five times. After that the spray is used once or twice a day only if necessary.

6. Fluids are forced strongly by mouth.

7. Hypodermoclysis of physiologic solution of sodium chloride is given every six or eight hours, as indicated by the patient's condition.

8. Fluids are given intravenously only if the temperature rises to 103 F.

9. Transfusion is done if necessary.

10. The patient is moved about as soon as the crust is established and is allowed to walk about as soon as the period of shock is over and if no signs of toxemia develop. The patient is gotten up and about regardless of the size or location of the burned area and usually may walk about freely after the first twenty-four hours if the burn is small, covering up to about 20 per cent of the body surface. It is perhaps safer to keep the patient with the more extensive burn in bed from five to seven days, or at least till the temperature has been normal for about twenty-four hours.

11. If any coagulum remains at the end of two and one-half or three weeks, it should be soaked off with brine or by compresses. Compresses treated with cysteine hydrochloride, 1:200 solution, may then be applied to the third degree areas that are not healed, alternating every four days with compresses soaked in boric acid or gauze treated with scarlet red may be applied to stimulate epithelization.

SUMMARY AND CONCLUSIONS

A treatment for extensive burns which employs silver nitrate and methyl rosaniline has been presented in detail.

During the experimental period ninety-five patients were treated with various combinations of solutions, and the mortality rate was only 7.3 per cent.

Since the establishment of the silver nitrate-methyl rosaniline therapy, eighteen additional patients have been treated, with no deaths. The data in these cases have been presented in detail.

A simple method of dealing with minor burns in ambulatory patients has been presented, methyl rosaniline being used in a water soluble base.

The principles set up for the treatment of burns with tannic acid have been upheld with this form of therapy, even though that solution was not used, and, in addition, there are several advantages.

Shock and pain were held at a minimum.

Toxemia rarely developed as a clinical threat.

Infection rarely became a severe complication, regardless of the location of the burned area.

Patients were moved about freely after the first few hours and were urged to get up in wheel chairs or to walk in a few days regardless of location of the coagulum or its extent.

Burns healed quickly; the period of hospitalization was very short.

Skin grafting was rarely, if ever, necessary to get the patient quickly covered with epithelium.

Scar tissue was held at a minimum.

Urinalyses done as a routine showed no renal complications.

The general outlook of the patients was extremely good as soon as the period of pain and fright was over.

1337 David Whitney Building.

MENINGOCOCCIC MENINGITIS COMPLICATING FRACTURE OF THE SKULL

EUGENE CLARK, M.D.

JULIUS REDISH, M.D.

AND

NORMAN JOLLIFFE, M.D.

NEW YORK

Acute purulent meningitis complicating fracture of the skull and caused by pyogenic cocci is well known, but meningococcic meningitis occurring under similar conditions has been infrequently reported. Four such cases have recently been observed at the Bellevue Hospital and are being reported because of their therapeutic indications and forensic importance.

A study of the relationship of trauma and fracture of the skull to meningococcic meningitis was reported by Seligmann and Pieper.¹ Of 674 cases of meningococcic meningitis, a history of trauma was recorded in 55, but fracture of the skull was demonstrated in only 2. In 21 of their cases, including the 2 in which there was fracture of the skull, meningitis appeared from one to three days after trauma. In 17 cases trauma preceded the onset of meningitis by from eight days to three months, and in 17 others a period of from four months to two years elapsed between trauma and the onset of meningitis. The authors asserted that in several of these cases the causal relationship between trauma to the head and meningococcic meningitis appeared unequivocal and that in the majority of the others the existence of this relationship was at least probable.

In 8 other cases a similarly long interval (from twelve days to eight months) is recorded between the time of trauma to the head² or frac-

From the Psychiatric Medical Service of the Third Medical Division (New York University) and the Department of Pathology, Bellevue Hospital, and the Office of the Chief Medical Examiner of the City of New York.

1. Seligmann, E., and Pieper, E.: *Die Cerebrospinalmeningitis in Preussen in den Jahren 1923 und 1924*, Veröffentl. a. d. Geb. d. Med.-Verwalt. **20**:441, 1926.

2. Reiche, F.: *Der senile Typus der übertragbaren Genickstarre*, München. med. Wchnschr. **56**:1829 (Sept. 7) 1909. Gutzeit, K., and Stern, R.: *Trauma und epidemische Meningitis*, Med. Klin. **25**:1400 (Sept. 6) 1929.

ture of the base of the skull³ and the onset of meningococcic meningitis. In other reports, however, the interval was briefer. In 7 cases⁴ meningococcic meningitis followed fracture of the skull within from one to eight days, and in 5 cases of trauma to the head but no fracture of the skull⁵ from one to four days elapsed before the development of meningococcic meningitis. In a case of trauma to the head with fracture of the nasal bones⁶ meningococcic meningitis was observed eighteen hours after the injury.

REPORT OF CASES

CASE 1.—M. Z., a 52 year old white man, was admitted to the psychiatric service on April 16, 1934, because of an injury to the head. He appeared acutely alcoholic and showed contusions of the nose, epistaxis and projectile vomiting. The temperature was normal, and the spinal fluid, bloody. On April 18 the temperature rose to 103 F., but the spinal fluid was unchanged. On April 19 the spinal fluid was xanthochromic. On April 21 there were stiffness of the neck and a positive Kernig sign, and the spinal tap revealed purulent fluid containing micro-organisms which were identified on culture as meningococci.⁷ Three addi-

3. Schmidt, P.: Pneumokokken- und Meningokokken-Meningitis nach Schädelbasisfraktur, Deutsche med. Wchnschr. **42**:124 (Feb. 3) 1916. Terbrüggen, R.: Ein weiterer Fall von epidemischer Zerebrospinalmeningitis nach Schädelbasisfraktur, Ztschr. f. Laryng., Rhin., Otol. **18**:312 (Aug.) 1929. Gruber, G. B.: Zur Lehre von Wesen, Verbreitung und Bekämpfung der Meningokokken-Meningitis, Ztschr. f. Hyg. u. Infektionskr. **80**:219 (Aug. 18) 1915. Lode, A., and Schmuttermayer, F.: Traumatische Meningokokken-Meningitis, Wien. klin. Wchnschr. **42**:5 (Jan. 4) 1929. Macgrath, B. G., and Adel, M. B.: Meningococcal Meningitis Following Fracture of the Skull, Lancet **1**:863 (April 13) 1935. Aronowitsch, G. D.: Meningitis und Trauma (Ueber Fälle von Meningokokken- und Pneumokokkenmeningitis nach Kopfverletzung), Deutsche Ztschr. f. Nervenhe. **129**:73 (Dec. 22) 1932.

4. Torrance, A. M.: Meningococcus Meningitis Following Head Injuries, Clin. Med. & Surg. **37**:898 (Dec.) 1930. Korbsch, H.: Meningitis cerebrospinalis epidemica nach Schädeltrauma, Arch. f. Psychiat. **70**:221, 1923-1924. Kalb, A.: Ueber Meningokokkenmeningitis nach Schädeltraumen, Beitr. z. klin. Chir. **124**:211, 1921. Voss, O.: Epidemische Zerebrospinalmeningitis im Anschluss an Schädelbasisfrakturen, Ztschr. f. Laryng., Rhin., Otol. **17**:221 (Dec.) 1928. Lindstrom, E.: Meningitis cerebrospinalis post traumam, Hygiea **5**:708 (July) 1905.

5. Busi, A.: Intorno a un caso di meningite cerebro-spinale traumatica, Arch. di psichiat. **26**:497, 1905. Richey, de W. G., and Helmbold, T. R.: A Case of Meningococcic Meningitis Following Head Injury, Am. J. M. Sc. **166**:559 (Oct.) 1923. Munk, W.: Den traumatiske purulent meningitis, Bibliot. f. læger **119**:218 (Feb.) 1927. Brändle, U.: Trauma und Meningitis, Dissert., Vienna, Holzworth and Berger, 1932. Jakob, F.: Posttraumatische Meningokokken-Meningitis, Schweiz. med. Wchnschr. **64**:630 (July 7) 1934.

6. Weitzel, L., and Martin, L.: Rechute de méningite cérébro-spinale après un traumatisme crânien, Presse méd. **34**:1211 (Sept.) 1926.

7. In all 4 cases the identification of the micro-organism was determined by fermentation and agglutination reactions.

tional cultures of the spinal fluid in the subsequent week confirmed the presence of meningococci, and although antimeningococcus serum was given intrathecally at daily intervals, death occurred on May 2, sixteen days after the patient's admission to the hospital.

Necropsy revealed a vertical fracture of the occipital bone with extension into the right petrous bone. There were contrecoup lacerations of the brain and subdural hemorrhage. A slight hemorrhage was encountered in the sphenoid sinus, but the ethmoid sinuses and middle ears showed no suppuration. There was an abundant collection of greenish purulent exudate over the vertex and the dorsal surface of the cerebellum.

CASE 2.—J. T., a 61 year old white man, was admitted to the psychiatric service on May 16, 1936. The patient was irrational and could give no account of himself. Examination disclosed abrasions over the occipital region of the scalp and contusions over the left frontoparietal area and left thigh. Caked blood was found in the nares. The temperature was 98.6 F., and the spinal fluid was bloody. During the first two days the patient remained confused and disoriented. On May 19 the temperature rose to 103.2 F., and stiffness of the neck and a positive Kernig sign were elicited. The spinal fluid was xanthochromic and contained many polymorphonuclear leukocytes and gram-negative intracellular diplococci, which were identified on culture as meningococci. Antimeningococcus serum was given daily by the intraspinal route, but the patient died on May 22, six days after admission to the hospital.

At necropsy a fracture of the skull was encountered which ran about $\frac{3}{4}$ inch (1.9 cm.) to the left of the occipital apex down into the foramen magnum and extended up between the vascular process in the occipital portion and the left temporal bone through the sella turcica longitudinally. There was a laceration of the brain on the under-surface of the frontal and temporal lobes on the right side. A leptomeningitis of the purulent type was found around the pons and the cerebellum.

CASE 3.—L. D., a 49 year old white man, was admitted to the psychiatric service on May 1, 1936. The patient was found on the street in a stupor, and no history could be obtained. Examination revealed dried blood in the nares and in the left external auditory canal. The temperature was 99.6 F., and the spinal fluid was bloody. During the next ten days the patient appeared rational and was afebrile, though he complained of headache. On the tenth day, because of persistence of the headache and the elevation of the temperature to 104 F., the spinal tap was repeated, and the fluid contained many polymorphonuclear leukocytes and gram-negative diplococci, which were identified on culture as meningococci. A daily spinal tap also showed the fluid to contain meningococci. The patient was daily given intraspinal injections of antimeningococcus serum and appeared to be doing well until acute parotitis developed. He died on June 2, thirty-two days after admission to the hospital.

At necropsy a transverse fissure fracture was noted in the petrous portion of the left temporal bone. The cells of the left middle ear and mastoid contained greenish yellow pus. The air cells of the right ear and mastoid and the right sphenoid and ethmoid sinuses were normal. Reddish brown discoloration of the dura was found over the right parietal and occipital regions. A greenish yellow purulent exudate was encountered in the cisterna magna.

CASE 4.—S. Z., a 27 year old professional wrestler, was admitted to the psychiatric service on June 1, 1936. On May 26, while engaged in a wrestling match, he was thrown out of the ring. Shortly thereafter he went to his hotel.

where he fell out of a second story window. No record is available of his course previous to the admission to the hospital, except that he had been disoriented and violent. On admission he appeared quiet and cooperative and presented multiple contusions. The spinal fluid was purulent and contained meningococci in pure culture. Antimeningococcus serum was given intrathecally, but deepening stupor appeared and death occurred forty hours after the patient's admission to the hospital. Culture of the final spinal puncture fluid yielded meningococci and type II pneumococci.

At necropsy a fissure fracture, about 1 cm. in length, was found in the petrous portion of the left temporal bone. Blood was encountered in the right middle ear, but the left middle ear, the mastoid cells and the sphenoid and ethmoid sinuses contained neither blood nor pus. A purulent leptomeningitis was present over the the vertex of the brain.

COMMENT

All 4 patients exhibited the coexistence of fracture of the skull and meningococcic meningitis. In cases 1, 2 and 3 the sequence of events appears clear, in that meningococcic meningitis followed fracture of the skull in five, three and ten days, respectively. In case 4 meningitis was present when the patient was first observed, and the sequence of events is therefore uncertain. It is possible but not probable that the patient had meningitis at the time of the wrestling match.

Although it is to be admitted that these 4 cases and the 16 cases reported in the literature are too few to establish definitely the direct causal relationship between fracture of the skull and meningococcic meningitis, certain considerations support this view. That the meninges may become readily invaded by pathogenic micro-organisms from the nasopharynx after fracture of the skull is well illustrated by the frequent cases of pneumococcic meningitis which occur following fracture of the base of the skull (Vance⁸). Therefore, when meningococci are present in the nasopharynx, it is to be expected that they too may invade and reach the subarachnoid space if the barrier between the nasopharynx and the meninges suffers injury. It is well known that meningococci are present in the nasopharynx of carriers and from time to time in otherwise normal persons.⁹ It is also known that the disease

8. Vance, B. M.: *Fractures of the Skull: Complications and Causes of Death; Review of Five Hundred and Twelve Necropsies and of Sixty-One Cases Studied Clinically*, Arch. Surg. **14**:1023 (May) 1927.

9. (a) Albrecht, H., and Ghon, A.: *Ueber die Aetiologie und pathologische Anatomie der Meningitis cerebrospinalis epidemica*, Wien. klin. Wchnschr. **14**: 984 (Oct.) 1901. (b) Zinsser, H., and Bayne-Jones, Stanhope: *A Text-Book of Bacteriology with a Section on Pathogenic Protozoa*, ed. 7, New York, D. Appleton-Century Company, Inc., 1934, pp. 443-446. (c) Rake, G.: *Studies on Meningococcus Infection: VI. The Carrier Problem*, J. Exper. Med. **59**:553 (May) 1934. (d) Tillett, W. S., and Brown, T. M.: *Epidemic Meningococcus Meningitis*, Bull. Johns Hopkins Hosp. **57**:297 (Nov.) 1935.

may ultimately develop in carriers who have harbored meningococci for some time without symptoms.¹⁰ Hence, it is reasonable to believe that meningococcic meningitis may appear in a carrier when fracture of the skull has created conditions suitable for invasion by the micro-organisms. That 3 of these cases were seen during the recent outbreak of meningococcic meningitis in New York¹¹ may be but a reflection of the presence of these micro-organisms in the nasopharynx in large numbers of the general population during epidemic periods.

In cases 1 to 3 the possibility is to be considered that the patient acquired the infection after admission to the hospital by contact with meningococcic carriers. Although there were no patients with meningococcic meningitis in the wards to which these patients were admitted, such patients were present in the other wards of the psychiatric medical service at the same time. This possibility, however, does not diminish the responsibility of the fracture of the skull in bringing about the meningitis. Although 30 cases of meningococcic meningitis have been observed in the wards of the psychiatric medical service of the Bellevue Hospital in the last eighteen months, no instance of contact infection of patients or hospital personnel has been observed. This is in accordance with the observations of others¹² on the extreme rarity of obvious infection from contact. However, in the recent outbreak in New York multiple cases of meningococcic meningitis were observed in 4 per cent of the families,¹¹ and in Baltimore^{9a} a history of contact was noted in 7 of 21 cases.

It appears possible from the case reports already cited¹³ that trauma may play a predisposing rôle in meningococcic meningitis without fracture of the skull. This receives some support from the experience of those who have observed the development of meningitis caused by the common pyogenic micro-organisms following trauma to the skull without fracture.¹⁴

10. MacCallum, W. G.: *A Text-Book of Pathology*, Philadelphia, W. B. Saunders Company, 1932, pp. 536-537. Zinsser and Bayne-Jones.^{9b}

11. Bolduan, C., and Frant, S.: The Recent Increase in Meningococcus Meningitis, *Quart. Bull. Dept. of Health, New York* 4:47, 1936.

12. Simon, C. E.: *Human Infection Carriers*, Philadelphia, Lea & Febiger, 1919, pp. 106-133. Zinsser and Bayne-Jones.^{9b}

13. Footnotes 1, 2 and 5.

14. (a) Weichselbaum, A., in Kolle, W., and Wassermann, A.: *Handbuch der pathogenen Mikroorganismen*, Jena, G. Fischer, 1903, vol. 3, p. 293. (b) Wechsler, I. S.: *A Text-Book of Clinical Neurology*, ed. 2, Philadelphia, W. F. Saunders Company, 1931, p. 370. (c) Finkelnburg, R.: *Die Erkrankungen der Meningen*, in Lewandowsky, M.: *Handbuch der Neurologie*, Berlin, Julius Springer, 1911, vol. 2, p. 1091. (d) Ehrnrooth, E.: Eitrige Meningitis, akut entstanden nach Kopftrauma ohne nachweisbare Wunde, *Deutsche Ztschr. f. d. gerichtl. Med.* 12:30 (Aug. 27) 1928.

Although in our cases of meningococcic meningitis a potential communication between the meninges and the nasopharynx was created by the fracture of the sphenoid bone in case 2 and of the petrous portion of the temporal bone in cases 1, 3 and 4, it is not known that the micro-organisms traveled along this route. It is possible that trauma to the meninges and the brain furnishes an area of diminished resistance for micro-organisms invading directly from the nasopharynx or from the blood stream. In this connection, Ehrnrooth^{14d} has shown in experimental animals that trauma to the head without fracture of the skull promotes the development of meningitis after the intravenous injection of micro-organisms. The rôle played in the propagation and dissemination of the meningococci by otitis and mastoiditis in case 3 and by hemorrhages in the sphenoid sinus in case 1 and in the middle ear in case 4 is not clear.

SUMMARY

Four cases are reported in which meningococcic meningitis followed fracture of the base of the skull. Attention is called to 16 similar cases reported in the literature, and the considerations are discussed which support the view that a direct causal relationship exists between fracture of the skull and meningococcic meningitis.

Drs. Thomas Gonzales, Benjamin Morgan Vance and Milton Helpert, of the Office of the Chief Medical Examiner, New York, supplied the necropsy records.

EFFECT OF STARVATION ON THE HEALING OF FRACTURES IN RABBITS

GRAHAM KERNWEIN, M.D.

CHICAGO

Prolonged abstinence from foods providing certain essentials to normal life processes results in various well known deficiency diseases which must be distinguished from changes arising in normal animals suddenly deprived of all food intake. For purposes of clarity the former may be regarded as changes arising from chronic starvation and the latter as those arising from acute starvation. It is with healing in diseases arising from acute starvation that this paper is concerned.

A review of the literature reveals that investigators unanimously agree that acute starvation does not inhibit either growth or repair. McCollum and his co-workers¹ demonstrated that fasting would cause active rickets in rats to heal from within twenty-four to forty-eight hours. Shipley and Holt² reported studies in vitro and stated that solutions to which 51.3 millimols of sodium chloride had been added inhibited calcification in preparations of the bones of rats with rickets, while similar preparations from starved rats calcified perfectly. Harvey and his co-workers,³ who studied the effect of starvation on fibroplasia and the healing of wounds in the stomach of the rat, found that starvation produced no change in the initiation of growth or in its velocity. Roegholt⁴ found that lack of vitamin A did not slow up the processes of healing in a wound. Morgan⁵ stated that the legs of starved salamanders regenerated after amputation as rapidly as those of normally fed animals.

From the Department of Surgery of the University of Chicago.

1. McCollum, E. V.; Simmonds, N.; Shipley, P. G., and Park, E. A.: *The Effect of Starvation on the Healing of Rickets*, Bull. Johns Hopkins Hosp. **33**:31, 1922.

2. Shipley, P. G., and Holt, L. E., Jr.: *Effect of Starvation on Healing of Rickets in Rats*, Proc. Soc. Exper. Biol. & Med. **25**:32, 1927.

3. Howes, E. L.; Briggs, H.; Shea, R., and Harvey, S. C.: *Effect of Complete and Partial Starvation on the Rate of Fibroplasia in the Healing Wound*, Arch. Surg. **27**:846 (Nov.) 1933.

4. Roegholt, M. N.: *Influence of Diet Free from Vitamin A on Myelopoiesis and the White Blood Picture and Its Effect on Wound Healing*, Nederl. tijdschr. v. geneesk. **2**:3744 (Aug. 10) 1929.

5. Morgan, Thomas H.: *The Physiology of Regeneration*, J. Exper. Zool. **3**:457, 1906.

There is even some evidence that cell division is stimulated by starvation, as Morgulis and his co-workers⁶ quoted Gaglio⁷ as finding mitotic figures more frequent in tissues from starved than in those from normal frogs and Morpurgo⁸ as finding the same for pigeons. Morgulis concluded from his studies that there is a reduction in cell cytoplasm in starved animals but little reduction in the nucleus. This disturbed ratio results in an increased rate of cell division in an effort to restore the proper balance. Harvey and his co-workers found in the rat that healing of well approximated clean wounds of soft parts is usually complete by fibroplasia in about fourteen days. However, healing of fractures involves more than repair by fibroplasia and requires a longer time. The callus that forms is at first fibrous and subsequently ossifies, partly by fibrous ossification and partly by enchondral ossification.

In order to test the effects of starvation on the phases of the healing of fractures, the following experiments were carried out.

EXPERIMENTAL WORK

Sixty-two adult rabbits of approximately the same age, weight and general physical condition were operated on, and the ulna was fractured by open operation about 1 inch (2.5 cm.) above the joint. No attempt at immobilization of the fracture was made. The animals were then divided into two groups. One group was fed the usual laboratory diet; the other group was placed in metabolism cages so that all excretions were immediately disposed of, and their intake was limited to a 0.9 per cent solution of sodium chloride. There was considerable variation in the ability of the animals to withstand starvation, as they succumbed at intervals ranging from nine to thirty-seven days. Control animals were killed at intervals corresponding in duration to those which succumbed to starvation. The specimens were dissected, roentgenograms were made and the specimens were then sectioned for microscopic examination.

RESULTS

RABBIT 745.—*Eighteen day fracture; normal diet.*

There was a large amount of external callus which was practically entirely ossified. Mesially both the radius and the ulna participated in the process of ossification. In the mesial external callus a large displaced fragment of cortex without nuclei was seen. New bone was being laid down on the dead fragment on two sides. Of the other two sides, the long side adjacent to the fibrous portion of the callus was without new bone, and the end in contact with the radius was necrotic and disintegrating, as was the contacting portion of the radius. The

6. (a) Morgulis, S.; Howes, P. E., and Hawk, P. B.: Studies on Tissues of Fasting Animals, Biol. Bull. 28:397, 1915. (b) Morgulis, S.: Fasting and Undernutrition: A Biological and Sociological Study of Inanition, New York, E. P. Dutton & Company, 1923.

7. Gaglio, G.: Sulle alterazioni istologiche e funzionali dei muscoli durante l'inanizione, Arch. per le sc. med. 7:301, 1884; cited by Morgulis.^{6b}

8. Morpurgo, B.: Sull processo fisiologico di neoformazione callulare durante la inanizione acute dell' organismo, Arch. per le sc. med. 12:395, 1888; cited by Morgulis.^{6b}

marked radial periosteal reaction ceased abruptly where contact with the dead fragment began. No cartilage was seen in the lateral external callus and only a small island in the mesial external callus. The fractured ends of the ulnar cortex were shredded and undergoing absorption, as evidenced by the large haversian canals.

The callus separating the opposing fragments of the ulnar cortex was ossified only in that region immediately surrounding the bone, leaving a wide strip of fibrous callus between the two ends. The medullary callus was a dense bony plate with a narrow unossified line in the center extending transversely across the medullary cavity. Numerous displaced spicules of cortical bone were present with new bone laid down on them. There was only a minimal amount of endosteal reaction present, it being most marked on the cortex next to the radius.

RABBIT 686.—Eighteen day fracture; starvation.

A thin line of lateral external callus was ossified except in the region of the fracture and a few millimeters of the adjacent cortex. Here there was a dense fibrous callus which separated the ends of the ulna and extended completely across the fracture defect. Disseminated throughout were spicules of cortical bone without nuclei and giant cells, some lying in contact with the dead bone.

There was no callus formation on the mesial side. In the interosseous region, between the ends of the fractured ulna and in the adjacent portion of the medullary cavity, was an acellular granular mass of necrotic tissue, representing the remains of an unabsorbed hematoma. The medullary callus was composed of a wide central band of moderately dense fibrous tissue with many large vacant spaces like those left where fat has been dissolved out during fixation. Peripherally, there were two bands of beginning ossification; the trabeculae here were thin and lacelike, and the cells were larger and closer together than those seen in the specimen from rabbit 745. There was a marked endosteal reaction present. The haversian canals of both the radius and the ulna were much larger than those in the specimen of rabbit 745, indicating osteoporosis.

Comment.—The specimen from the starved animal could be identified microscopically by the lesser amount of external callus, lack of ossification of both the external and the medullary callus, the spongy nature of the ossification present and the presence of osteoporosis.

RABBIT 737.—Twenty-two day fracture; normal diet.

The lateral external callus was ossified except for the region between the fragments of the fractured ulna. A small island of cartilage was attached to each of the fragments. The ossification of the mesial callus was limited to the few millimeters adjacent to the cortex of the radius and the ulna. The region immediately adjacent to the fracture line was cartilaginous, and between this cartilage and the fractured ulna were two small pieces of necrotic and disintegrating cortex. The fragments were in good alignment, and in the first few millimeters adjoining the fracture line no nuclei were seen. The region between the two ends contained a small amount of an acellular and granular material, representing an unabsorbed hematoma. On the medullary cavity side of the fracture line was a piece of necrotic disintegrating bone completely surrounded by a large island of cartilage and new bone which spanned the defect.

The medullary callus was ossified peripherally, forming two wide bands of dense bone which stretched transversely across the medullary space and were separated from one another by a narrow band of unossified callus, fibrous in the lateral half and cartilaginous in the mesial half. Spicules of displaced dead cortical

bone with new bone laid down on them still remained. The endosteal reaction and ossification of the callus were more marked mesially than laterally.

RABBIT 681.—*Twenty-two day fracture; starvation.*

The lateral external callus was only partially ossified, being most marked in the cortical region of the proximal fragment. Mesially, ossification of the callus was occurring on the surface of both the radius and the ulna. There was a medullary callus at the site of the fracture which was cartilaginous in the intermediary zone and ossified distal to this in the ends of the fragments. It contained some spicules of dead bone that had been crushed into the cavity by the cutting forceps. Their cells had disappeared, and there was irregular formation of new bone on their surfaces.

Comment.—There was no doubt that both fractures were healing, but that healing was delayed in the starved animal was attested by a lack of ossification of the external callus, relatively less ossification of the medullary callus, lack of endosteal reaction and less actively appearing fibrous callus as compared with the specimen from the normal animal.

RABBIT 679.—*Twenty-nine day fracture; normal diet.*

The callus was completely ossified, forming a dense spongy plate of bone which united the fragments of the ulna. Between the fractured ends an acellular granular precipitate was seen, again representing the remainder of an unabsorbed hematoma. The cortices of the ends of the fragments were without nuclei for a short distance away from the fracture line. The periosteum of the radius in the neighborhood of the fracture had formed a layer of new bone.

The medullary callus was ossified except for one small island of cartilage. The ossified callus formed a wide plate of dense new bone composed of thick wavy trabeculae with small marrow spaces. In the meshes of this new bone lay numerous spicules of dead cortex undergoing bony transformation by creeping substitution.

RABBIT 683.—*Twenty-nine day fracture; starvation.*

The soft tissues attached along the lateral side were densely fibrous and included portions of tendons and muscle. That portion near the fracture line and in the periosteal regions was ossified. A large spicule of dead cortex lay out in the periphery of the lateral callus surrounded by dense fibrous tissue, except on one end. Here there was an island of cartilage with cartilage cells invading the dead spicule. The fragments of the ulna were dead for from 1 to 5 mm. away from the fracture line. A fibrous callus separated the fragments, ossification being limited to that portion immediately about the surface of the fracture.

There was no callus formation on the radial side. Here the fragments were in good alinement, and in the intervening space was a necrotic granular mass of tissue. The fragments were dead in the portions adjoining the fracture line and were undergoing absorption. The medullary callus was separated into two parts by a band of fatty marrow. That part associated with the lateral fragments of the ulna was composed of a central band of dense fibrous tissue continuous with the lateral callus and ossified peripherally where dead spicules of cortex were also being transformed. Here there was only a minimal amount of endosteal reaction. On the radial side a well marked endosteal reaction formed a hillock of new bone, which completely spanned the cortical defect. In the center of

this hillock and spanning the fracture defect lay an island of cartilage. The ossification on the distal fragment was by spongy bone, and here there were many multinucleated giant cells. On the proximal fragment the bony trabeculae were heavier, and only a few giant cells were present.

Osteoporosis of the fragments of both the radius and the ulna was marked. The large number of giant cells present was an outstanding feature.



Fig. 1.—Section of a thirty-three day fracture of the ulna (*u*) of a rabbit on a normal diet. The callus is ossified. The radius is indicated by *r*.

Comment.—The specimen from the animal on a normal diet showed bony union, while that from the starved animal showed a callus that was partly ossified, and the bone was more spongy than that of the first specimen. The specimen from the starved animal showed marked osteoporosis.

RABBIT 239.—*Thirty-three day fracture; normal diet.*

A band of almost completely ossified callus united the fragments of the ulna and formed a wide bony bridge, which extended transversely across the medullary canal. A few cartilage cells were present in the intermediary callus. A few fragments of displaced cortical bone without nuclei lay scattered throughout this bony callus and were completely surrounded by living bone which had been

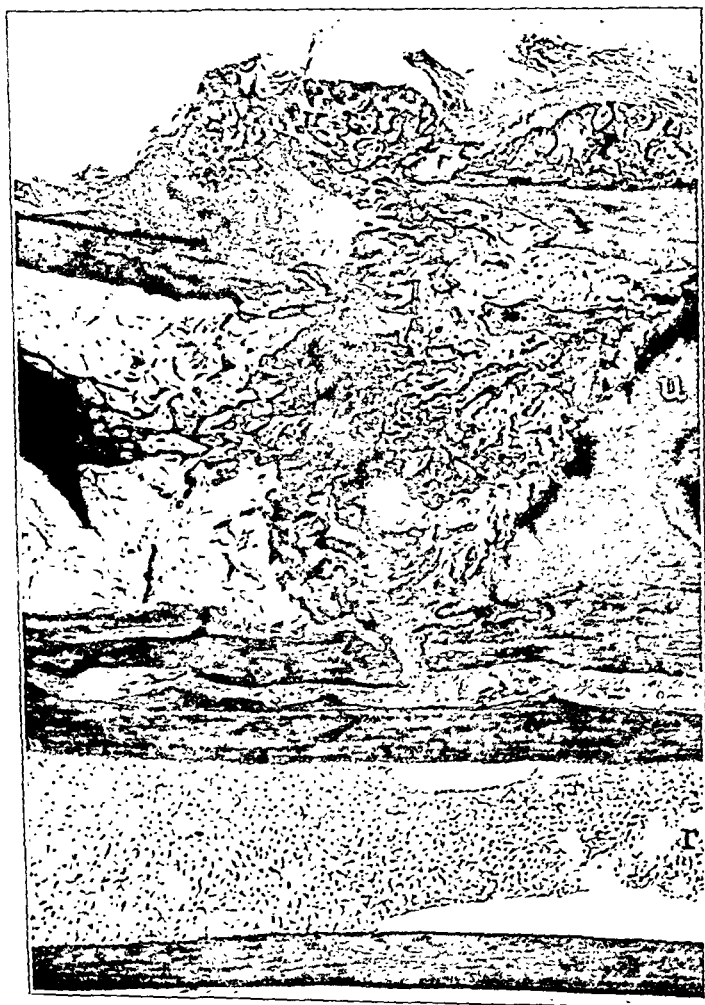


Fig. 2.—Section of a thirty-three day fracture of the ulna of a starved rabbit. The intermediary callus is fibrocartilaginous, and the bony callus is less dense than that in the control specimen (fig. 1). The ulnar (*u*) and radial (*r*) cortices were osteoporotic.

deposited on them. The mesial cortex was united so well that if it were not for a large piece of dead cortical bone extending at an angle of 45 degrees into the medullary cavity and still attached at one end, one might doubt that a fracture had ever been present.

RABBIT 321.—*Thirty-three day fracture; starvation.*

The lateral callus was ossified by a spongy type of bone. Between the ends of the fragments the fibrous callus remained unossified. There was no mesial callus formation, and the fragments here were not united, the intervening space being filled by tissue like the marrow elsewhere in the specimen. The ossification of the medullary callus was by a spongy type of bone, and extending transversely across the medullary cavity was a band of unossified callus composed about equally of fibrous tissue and cartilage. Marked osteoporosis was present. Giant cells and mononuclear cells were present in the dilated canals and along the surfaces of the cortex and also in the spongy bony callus, indicative of absorption of both the old and the new bone.

Comment.—These two specimens present a sharp contrast, revealing conclusively the inhibiting effect on bony union of acute starvation. The specimen from rabbit 239, the normal animal, shows a healed fracture; that from rabbit 321, the starved animal, shows an ununited fracture with the fracture line wide open, retarded ossification by a spongy bone and marked osteoporosis.

RABBIT 242.—*Thirty-four day fracture; normal diet.*

The ends of the fragments were united by densely ossified callus. The peripheral callus was small and roughly spindle shaped, and the medullary callus extended across the fracture line. It consisted of dense trabeculated bone, and there were a few giant cells and osteoblasts present, indicative of transformative activity.

RABBIT 246.—*Thirty-four day fracture; starvation.*

The ends of the fragments were connected by an unossified callus. Practically no periosteal callus was present. The intermediary callus was largely fibrous and the remainder cartilaginous. The endosteal callus was limited in amount and consisted of spongy bone. Disseminated throughout the fibrous intermediary callus were spicules of dead cortical bone undergoing absorption and not associated with any new bone formation. Osteoporosis was again marked. The same absorptive activity of old and new bone by mononuclear and giant cells was seen as in the section from animal 321.

Comment.—Again the difference in the specimens is striking. The specimen from the normal animal showed bony union of the fracture; that from the starved animal showed marked delay in ossification of the callus and marked osteoporosis.

RABBIT 349.—*Thirty-seven day fracture; normal diet.*

The lateral cortex was comminuted. A large spicule of cortical bone without nuclei lay diagonally across the fractured region at an angle of about 35 degrees but united at both ends with the neighboring fragment. New bone was being deposited on it by creeping substitution. There was a completely ossified mesial external callus, and the periosteum of the radius had formed a layer of new bone in the region of the fracture. All that remained of the medullary callus were two long narrow strips of bone without nuclei. They resembled displaced cortical bone which had not been absorbed. The only remaining fibrous callus was in a small region just beneath the dead and angulated cortical fragment previously mentioned. The fracture line on the mesial side could be identified with difficulty.

RABBIT 347.—Thirty-seven day fracture; starvation.

The fracture on the radial side was united by a callus that was fairly extensive and consisted of spongy bone, except for two small regions of cartilage in the intermediary zones at the limits of a splinter. On the opposite side and in the region of the medulla the callus was fibrous in its intermediary portion. There was a thin layer of ossified endosteal callus bordering on the intermediary callus. The cortex of the ends of the fragments on this side had been extensively absorbed and partly replaced by new bone, and there was a thin layer of periosteal, spongy bony callus on the proximal fragment.

Comment.—The specimen from the normal animal was healed. That from the starved animal was united mesially by a spongy type of new bone, and laterally there was fibrous union. Ossification of medullary callus was only minimal and again chiefly in conjunction with displaced dead cortical spicules.

COMMENT

In normal adult animals the formation and the destruction of bone are in equilibrium. Fracture of a bone in such an animal, however,

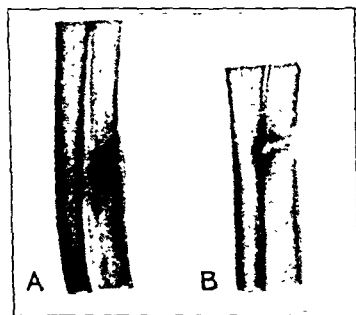


Fig. 3.—Roentgenograms of thirty-four day fractures of the ulna: *A*, a specimen from an animal on a normal diet, and *B*, a specimen from a starved animal.

disturbs the equilibrium locally and causes a shift favoring the formation of bone. Fibroplasia appears in both the periosteal and the endosteal region and proceeds to the formation of a fibrous callus, which later ossifies. The histogenesis of the bone which forms as a result of both enchondral and membranous ossification of the newly formed fibrous callus is complex, for fibroblasts must undergo metaplasia into chondroblasts and osteoblasts, and some of the cartilage is replaced by invading new bone. Complete ossification of the callus eventually takes place.

Suppression of any one or all of these various phases would tend to reverse the equilibrium and thus result in retarded healing time or, if severe enough, lead to nonunion.

Fractures produced in the normally fed rabbits required between three and four weeks for complete ossification of the callus, whereas in none of the fractures in the starved animals was ossification complete, although eleven survived over four weeks. In fact, fractures in

those animals which survived starvation more than thirty days showed less bony callus than did those from animals which succumbed to starvation in from twenty to twenty-six days.

One concludes, therefore, that acute starvation suppresses to some degree the process of ossification of the callus.

Comparison of the specimens from both starved and normally fed animals revealed no obvious difference in the time of appearance or

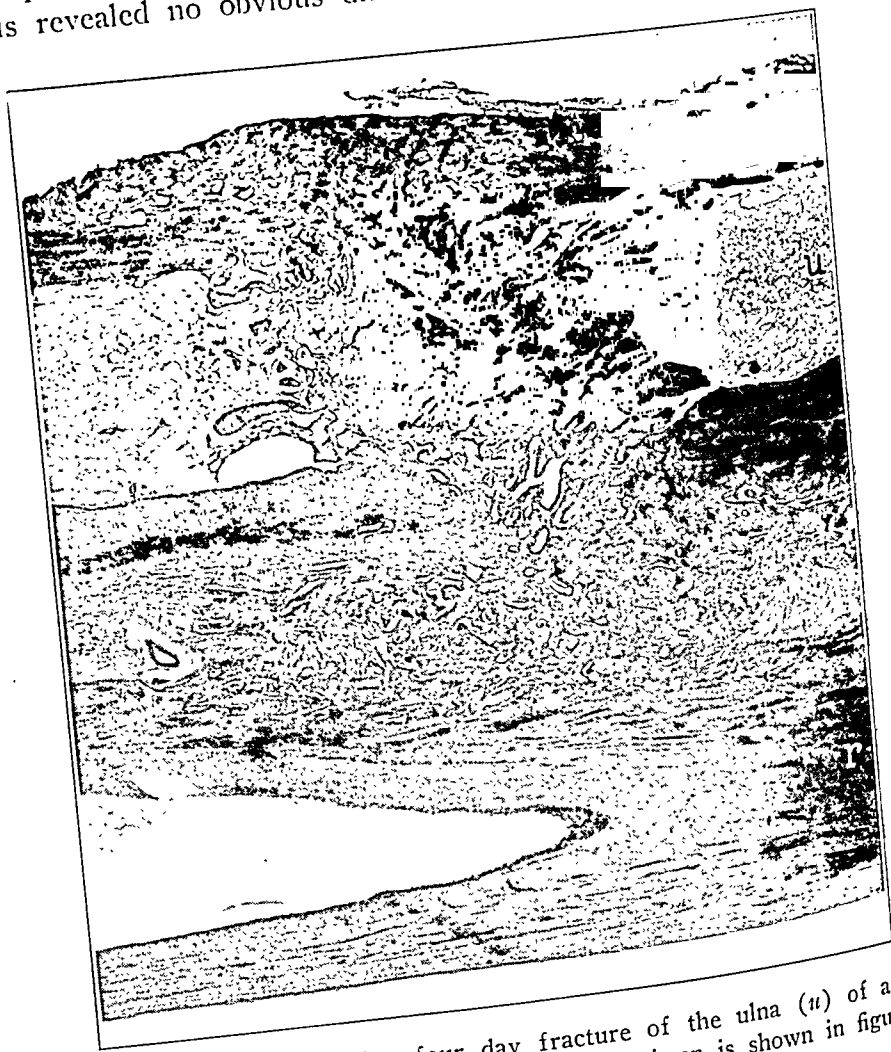


Fig. 4.—Section of a thirty-four day fracture of the ulna (*u*) of a rabbit on a normal diet. The roentgenogram of this specimen is shown in figure 3*A*. The callus is ossified. The radius is indicated by *r*.

completion of fibroplasia. Local factors, such as the amount of comminution, approximation of the fragments and disturbance of the periosteum, determine largely the amount of callus formed. Initiation and completion of fibroplasia and the amount of callus formed are therefore not affected by acute starvation. This observation agrees with that of Harvey and his co-workers, who could demonstrate no retarding effect of starvation on fibroplasia in well approximated clean wounds in soft tissue.

Starvation, then, must affect only the process of ossification. This may be accomplished in one or all of three ways, i. e.: by (1) inhibiting the metaplasia of fibroblasts into chondroblasts and osteoblasts; (2) by restricting the bone-forming activity of chondroblasts and osteoblasts to a minimum, or, since the retarding effect was proportional to the duration of the period of starvation, (3) by a shift of the equilibrium

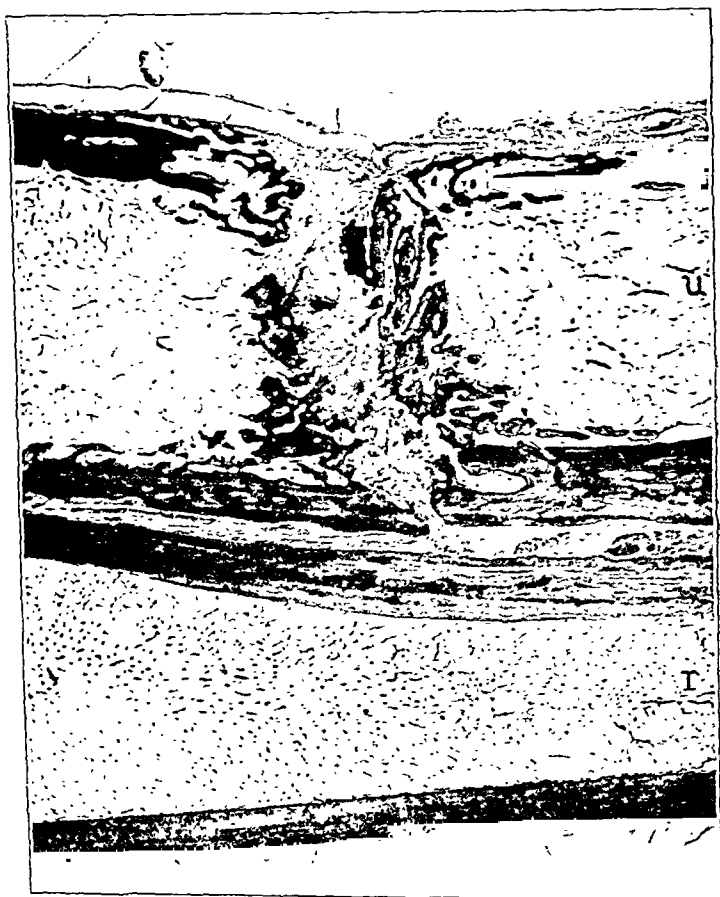


Fig. 5.—Section of a thirty-four day fracture of the ulna (*u*) of a starved rabbit. The roentgenogram of the specimen is shown in figure 3 *B*. The callus is smaller than that in the control specimen (fig. 4). The intermediary callus is fibrocartilaginous, and the bony callus is spongy. The ulnar cortex is markedly osteoporotic, and the radial cortex, less so.

so as to accelerate the destruction of bone at the expense of the formation, in which case one would expect to see a preponderance of osteoclasts resulting in an absorption of the newly ossified callus and a generalized osteoporosis.

Comparison of the specimens from starved and fed animals revealed that metaplasia had occurred in both, for both enchondral and membranous ossification were present. However, the older specimens from the starved animals could be distinguished from those from fed animals by (1) the relatively lesser amount of ossification and (2) the more spongy character of the bone that had been laid down. Generalized osteoporosis was present in the specimens from starved animals, almost from the beginning of ossification of the callus, but was much more marked in the specimens from animals which survived thirty days or more. In addition, the specimens from the latter actually exhibited many osteoclasts, lacunar absorption and less ossification than was seen in specimens from animals succumbing after from twenty to twenty-six days.

One can only surmise as to the actual mechanism of the retarding effect of starvation on ossification of the callus. It would seem, however, that in the beginning starvation chiefly inhibits metaplasia of the fibroblasts and limits the activity of the chondroblasts and osteoblasts to a minimum, so that healing progresses along a fairly normal but definitely inhibited course up to about twenty-six days. Thereafter the constantly increasing shift of equilibrium favoring the destruction of bone (as evidenced by the mild osteoporosis present) seems to be accelerated, osteoporosis increases and osteoclasts and lacunar absorption are seen in the ossified callus.

CONCLUSIONS

1. The healing of a fracture was definitely inhibited by starvation.
2. The process of healing was normal during the stage of the formation of a fibrous callus. But in animals that survived this stage there was definite retardation of ossification of the callus, which became more marked with an increase in the length of the survival period.
3. Generalized osteoporosis gradually developed, and in the animals that survived longest there was some osteoporosis in the callus that had previously ossified.

EFFECT OF ANESTHESIA ON THE BLOOD OXYGEN

II. A STUDY OF THE EFFECT OF SPINAL ANESTHESIA ON THE OXYGEN IN THE ARTERIAL AND IN THE VENOUS BLOOD

JOHN L. SHAW, M.D.

BRANDT F. STEELE, M.D.

AND

CHARLES A. LAMB, M.D.

BOSTON

In a preceding communication¹ the existence of anoxic anoxia during ether anesthesia was demonstrated. Spinal or subarachnoid anesthesia is used frequently in surgical procedures, and it is therefore desirable to investigate the effects of spinal anesthesia on the oxygen in the arterial and in the venous blood.

Seevers and Waters² stated that the oxygen content in the arterial and in the venous blood is lowered during spinal anesthesia. However, they used large enough doses of drugs to produce respiratory paralysis, which rarely occurs in clinical surgical procedures. They did not present any data to show the degree of change in the blood oxygen. On the other hand, Nowak noted no significant changes in the oxygen of the arterial blood of cats under spinal anesthesia.³

In the present investigation we have undertaken to confirm and extend the observations of the previous investigators on the oxygen in the arterial and in the venous blood during a surgical spinal anesthesia.

METHODS

Dogs were used. A lumbar laminectomy was performed two or three days previous to the experiment, to facilitate the performance of a subarachnoid injection of procaine hydrochloride. It was found after several trials of direct injection that this was the most certain method of obtaining spinal anesthesia.

From the Surgical Research Laboratory and the Fifth Surgical (Harvard) Service, the Boston City Hospital.

1. Shaw, J. L.; Steele, B. F., and Lamb, C. A.: The Effect of Anesthesia on the Blood Oxygen: I. A Study of the Effect of Ether Anesthesia on the Arterial and Venous Blood Oxygen, to be published.

2. Seevers, M. H., and Waters, R. M.: Respiratory and Circulatory Changes During Spinal Anesthesia, *J. A. M. A.* 99:961 (Sept. 17) 1932.

3. Nowak, S. J. G.: To be published.

The animal was placed in a supine position on the operating board. Under anesthesia with procaine hydrochloride the vena cava was catheterized via the external jugular vein, and the femoral artery was prepared as outlined in a previous communication.¹ After the animal was allowed to become perfectly quiet and adjusted to the surroundings, the pulse and respiratory rates and the blood pressure were recorded. The samples of arterial and of venous blood were taken from the femoral artery and the catheter in the vena cava, respectively.¹ The samples were drawn anaerobically, stored under liquid petrolatum and preserved in an ice bath while the oxygen determinations were being made. Potassium oxalate was used as an anticoagulant.

The animal was then turned on its left side and the laminectomy wound gently opened to expose the dura. This was done without causing the animal any apparent pain or distress. The dog's dura is extremely sensitive, and a puncture cannot be made without producing pain; so before a solution of procaine hydrochloride could be injected into the subdural space it was necessary to administer ethyl chloride for anesthesia for about twenty seconds. While the dog was under ethyl chloride anesthesia a solution of from 10 to 20 mg. of procaine hydrochloride per kilogram of body weight in 1 or 2 cc. physiologic solution of sodium chloride was injected into the subdural space by means of a small needle bent at a right angle. The solution was colored with a few drops of gentian violet in order to make any leakage detectable. Immediately after the injection the ethyl chloride was withdrawn and the animal allowed to recover from the anesthesia. This usually occurred in from sixty to ninety seconds. The animal was then turned back to the supine position. Anesthesia usually began immediately, and the level was noted by testing the skin with forceps or a sharp instrument.

Samples of arterial and of venous blood were taken, and the blood pressure and the pulse and respiratory rates determined after periods of thirty minutes and one hour, respectively. The animals were killed at the end of the experiment by quick intravenous injection of 100 mg. of sodium amytal per kilogram of body weight. Death occurred almost instantly. The trachea was exposed and clamped, and an immediate postmortem examination of the lungs was made.⁴

Blood oxygen determinations were made by the technic of Van Slyke and Neill.⁴

RESULTS

Eight experiments were performed. The results of the blood oxygen determinations for the experiments are recorded in tables 1 and 2 and shown graphically in charts 1 and 2.

The oxygen capacity of the arterial blood showed equivocal changes, though it tended to show changes of greater magnitude when decreasing.

In five of the eight experiments there was an increase in the oxygen content of the arterial blood. The greatest increase was 8.5 per cent. and the greatest decrease was 15.2 per cent. The mean change for the group was a slight increase.

4. Van Slyke, D. D., and Neill, J. M.: *The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement*. J. Biol. Chem. **61**:523. 1924.

TABLE 1.—Oxygen Values in Arterial and in Venous Blood of Dogs Under Spinal Anesthesia

Experiment No.	Oxygen Capacity of Arterial Blood				Oxygen Content of Arterial Blood				Oxygen Content of Venous Blood				Arteriovenous Difference				Oxygen Saturation of Arterial Blood*				Oxygen Saturation of Venous Blood*			
	Blood Sample After Anesthesia				Blood Sample After Anesthesia				Blood Sample After Anesthesia				Blood Sample After Anesthesia				Blood Sample After Anesthesia				Blood Sample After Anesthesia			
	Control Blood	30 Min.	1 Hour		Control Blood	30 Min.	1 Hour		Control Blood	30 Min.	1 Hour		Control Blood	30 Min.	1 Hour		Control Blood	30 Min.	1 Hour		Control Blood	30 Min.	1 Hour	
	Volumes per Cent	Volumes per Cent	Volumes per Cent	Volumes per Cent	Volumes per Cent	Volumes per Cent	Volumes per Cent	Volumes per Cent	Volumes per Cent	Volumes per Cent	Volumes per Cent	Volumes per Cent	Volumes per Cent	Volumes per Cent	Volumes per Cent	Volumes per Cent	Per-centage	Per-centage	Per-centage	Per-centage	Per-centage	Per-centage	Per-centage	Per-centage
1	21.0	26.1	20.2	23.0	25.2	24.8	17.1	18.6	17.4	5.9	0.6	7.4	92.4	95.5	91.0	68.8	70.5	66.4		68.8	70.5	66.4		
2	21.0	15.5	15.4	13.4	13.9	14.3	8.8	4.8	3.8	4.6	0.1	10.5	84.0	89.7	92.9	55.0	30.9	24.7		55.0	30.9	24.7		
3	16.0	10.7	17.2	16.2	16.0	15.9	11.1	7.9	8.2	5.1	8.1	7.7	91.5	95.8	92.4	62.7	47.3	47.6		62.7	47.3	47.6		
5	17.7	23.6	22.8	21.1	21.4	20.9	10.7	12.2	11.5	10.4	9.2	0.4	93.5	90.7	91.7	47.5	51.8	50.4		47.5	51.8	50.4		
6	22.0	17.9	17.6	19.0	10.8	10.1	15.0	6.9	5.9	3.1	0.9	10.2	91.3	93.8	91.5	75.0	38.7	33.5		75.0	38.7	33.5		
7	29.8	17.4	17.7	17.9	17.3	17.2	12.0	4.3	9.6	5.9	13.0	7.6	90.4	92.4	97.2	61.0	24.0	54.3		61.0	24.0	54.3		
8	10.7	16.5	16.6	14.4	15.0	14.5	9.8	8.0	...	4.6	7.0	...	88.9	90.7	87.3	60.5	48.5	...		60.5	48.5	...		
10	10.2	14.1	14.1	12.8	13.8	13.9	9.2	7.2	7.0	3.0	0.6	6.3	92.2	95.8	94.5	66.2	50.0	53.9		66.2	50.0	53.9		
11	13.9	14.1																						
Mean percentile change for the experimental series	-2.31	-2.71			+1.31	+0.47		-23.14	-20.65		+78.12	+75.92		+3.47	+2.83		-16.7	-15.05						
Mean variation of the mean percentile change †	±4.39	±5.69			±5.78	±7.44		±19.50	±21.30		±59.28	±58.75		±2.35	±3.60		±13.17	±14.51						
Mean of the mean variation of the mean percentile change	±1.55	±2.01			±2.05	±2.63		± 0.89	± 7.53		±22.43	±20.70		±0.83	±1.21		± 1.05	± 5.14						

* In the computation of the oxygen saturation of the arterial and venous blood, 0.5 and 0.3 volumes per cent were deducted from the oxygen capacity of the arterial blood and the oxygen content of the arterial and venous blood, respectively, to correct for the dissolved oxygen not in combination with the hemoglobin. The oxygen capacity of the arterial blood was used to calculate the oxygen saturation of the venous blood for general comparison, since the venous oxygen capacity of the venous blood was not ascertained in all instances.

In seven of the eight experiments there was a decrease in the oxygen content of the venous blood, the greatest decrease being 64 per cent. In one experiment there was an increase of 14 per cent in the oxygen content.

The arteriovenous difference increased sharply in seven of the eight experiments. In the one experiment in which no increase was recorded the initial arteriovenous difference was abnormally high.

In seven of the eight experiments an increase in the oxygen saturation of the arterial blood was noted. The greatest increase noted was 9 per cent and the smallest 0.4 per cent. In a single experiment a decrease in saturation of 2.8 per cent was recorded.

TABLE 2.—*Oxygen Values in Blood Samples Taken from Different Regions of the Body * (Experiment 8)*

Time of Taking Blood Sample	Blood Oxygen	Site of Blood Sample			
		Femoral Artery	Right Side of Heart†	Femoral Vein	External Jugular Vein
Control	Content (volumes per cent).....	17.9	12.0	11.1	12.4
	Capacity (volumes per cent).....	19.7	20.3		62.8
	Percentage of saturation.....	91.0	61.0	56.4	
30 minutes	Content (volumes per cent).....	17.3	4.3	8.2	7.9
	Capacity (volumes per cent).....	17.4	18.6		45.7
	Percentage of saturation.....	99.7	24.6	47.4	
1 hour	Content (volumes per cent).....	17.2	9.6	10.0	8.9
	Capacity (volumes per cent).....	17.7	19.1		50.5
	Percentage of saturation.....	97.7	54.3	56.4	

* The oxygen capacity of the arterial blood was used in computing the oxygen saturation of the venous blood for general comparison, since oxygen capacity of the venous blood was not determined in all the experiments.

† This sample of blood was taken from the junction of the superior and the inferior vena cava, as outlined under "Methods." It is not truly blood from the right side of the heart, but for practical purposes it should be almost identical.

In six of the eight experiments there was a decrease in the oxygen saturation of the venous blood. In two experiments small increases in the oxygen saturation were recorded, the largest of which was 4.3 per cent.

Table 2 shows the values for the samples of blood taken from different sources. The blood from the anesthetized area shows a slightly higher oxygen content than that taken from the upper part of the body. The difference is not marked and is well within the range of experimental variation.

There was no change in the blood pressure in experiment 5. In experiment 7 there was an increase in the blood pressure of 5.6 and 7.5 per cent for the thirty minute and one hour periods, respectively. Changes in the blood occurred in these experiments in spite of the

failure of the blood pressure to drop. The average changes for the five experiments were 37.5 and 31.1 per cent for the thirty minute and one hour periods, respectively. The lowest blood pressure reached was 40 mm. of mercury, a decrease of 71 per cent from the control.

The respiratory rate showed equivocal changes, though it tended to increase slightly and usually became shallower and largely diaphragmatic.

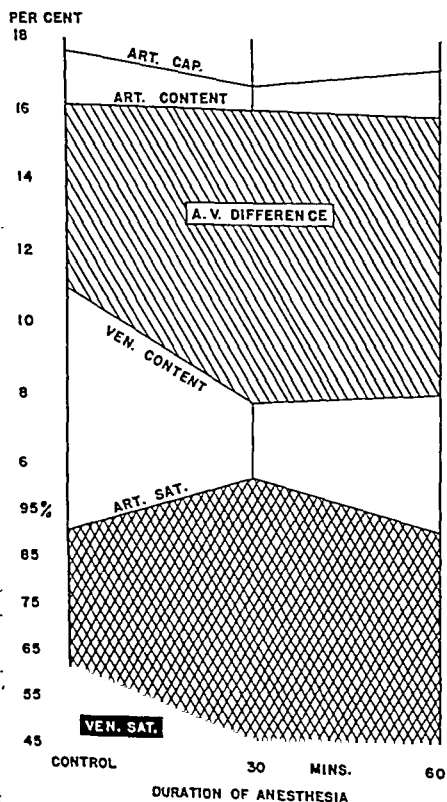


Chart 1

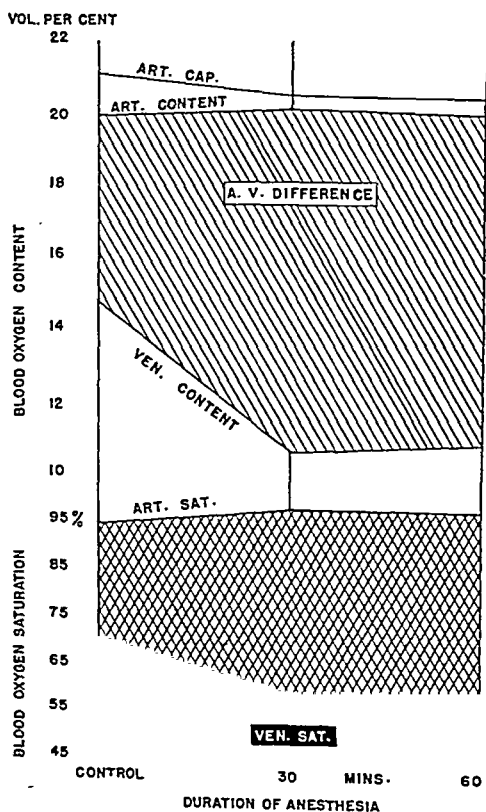


Chart 2

Chart 1.—Blood oxygen determinations in experiment 5.

Chart 2.—Mean of the results of the experimental series. The values used in this chart were calculated by use of the mean percentile changes for the experimental series, and as the control the following normal values for human blood were used: oxygen capacity of the arterial blood, 20.9 volumes per cent; oxygen content of the arterial blood, 19.9 volumes per cent; oxygen content of the venous blood, 14.9 volumes per cent; arteriovenous difference, 5 volumes per cent; oxygen saturation of arterial blood, 95 per cent, and oxygen saturation of venous blood, 71.4 per cent.

On postmortem examination the lungs appeared well inflated and evenly colored, except for a few small areas in the most dependent portions of the bases of the lungs, which were bright red. The striking feature about the lungs was their unusual paleness—a whitish pink—as if they were almost drained of their normal blood content. Removal of the tracheal clamp allowed the lungs to collapse without any areas of diminished crepitation. Gross section showed nothing remarkable, and no fluid could be expressed from the cut surface. The results of the microscopic examination were negative except for sparsely filled capillaries.

COMMENT

It is apparent that spinal anesthesia in the dog produces the following changes:

1. An increase in the oxygen saturation of the arterial blood. This change may be explained by the finding of a diminished content of the pulmonary blood, as indicated by the postmortem paleness of the lungs and a prolonged time for circulation of pulmonary blood.⁵ The diminished flow of pulmonary blood plus the exposure of a smaller quantity of blood than normal to the entire capillary-alveolar bed of the lungs insures the complete oxygenation of the arterial blood.

2. A decrease in the oxygen content of venous blood. This change is due to stasis and is found in such conditions as shock⁶ and cardiac decompensation. The blood from the right side of the heart may be considered as coming from two sources: the upper, unanesthetized, and the lower, anesthetized, area of the body. Its blood content will be the resultant of the mixture of blood from these two sources. Determinations on the oxygen in blood specimens taken simultaneously from each area of the body should give the source of the stasis. The results in experiment 8, shown in table 2, demonstrate that stasis occurs in both these regions of the body and appears to be slightly greater in the upper, unanesthetized, portion. The low oxygen content of venous blood in the upper, unanesthetized, part of the body is due to the reduced blood flow resulting from a compensatory vasoconstriction necessary to maintain a normal blood pressure. In conformity with the conception of an increased flow of blood through the anesthetized portion of the body due to the vasodilatation from vasoconstrictor

5. Nowak, S. J. G.: Personal communication to the authors. Shaw, J. L.; Steele, B. F., and Lamb, C. A.: Unpublished data on dogs using the sodium cyanide method.

6. Aub, J. C., and Cunningham, T. D.: Studies in Experimental Traumatic Shock: II. The Oxygen Content of the Blood, *Am. J. Physiol.* 54:408, 1920; 1921.

paralysis,⁷ it would be expected that the oxygen content of the venous blood would be normal or elevated. On the contrary, it was observed to be lowered. The vasodilatation in the anesthetized area of the body, unlike the arteriolar dilatation seen when ether anesthesia is used,⁸ involves the arterioles, capillaries and venules as a result of complete paralysis of their innervation. Since Krogh⁹ has shown that under normal circumstances only a small proportion of the capillaries are used at any one time, this vasodilatation, assisted by the paralysis of the voluntary muscles, enlarges the vascular bed and results in the shifting or pooling of part of the blood volume in the anesthetized part of the body. Bradshaw¹⁰ has shown that this vasoconstrictor paralysis is responsible for the fall in blood pressure observed in spinal anesthesia. Burch and Harrison¹¹ have demonstrated that as a sequel to a fall of 30 per cent or more in blood pressure the return of venous blood to the right side of the heart becomes inadequate, and a decreased cardiac output follows.

It is evident in the animals showing a fall in blood pressure that the pooling of blood from the vasodilatation in the region of anesthesia plus a diminished cardiac output and lowered blood pressure may produce a stasis of sufficient magnitude to explain the low oxygen content of the venous blood. The pale, blanched-appearing lungs may be further evidence of poor venous return to the heart from peripheral pooling.

The findings in the blood from the right side of the heart in the two experiments in which there was an increase and no change, respectively, in the blood pressure could be explained by a generalized vaso-

7. White, J. C.: Diagnostic Novacaine Block of the Sensory and Sympathetic Nerves: Method of Estimating Results Which Can Be Obtained by Their Permanent Interruption, *Am. J. Surg.* **9**:264, 1930. Morton, J. J., and Scott, W. J. M.: The Measurement of Sympathetic Vasoconstrictor Activity in the Lower Extremities, *J. Clin. Investigation* **9**:235, 1930. White, J. C.: Diagnostic Blocking of Sympathetic Nerves to the Extremities with Procaine: Test to Evaluate the Benefit of Sympathetic Ganglionectomy, *J. A. M. A.* **94**:1382 (May 3) 1930. Burch, J. C., and Harrison, T. R.: The Effect of Spinal Anesthesia on Arterial Tone, *Arch. Surg.* **22**:1040 (June) 1931.

8. Embley, E. H.: Action of Ether upon the Circulation, *Biochem. J.* **4**:79, 1910.

9. Krogh, A.: *The Anatomy and Physiology of Capillaries*, New Haven, Conn., Yale University Press, 1922.

10. Bradshaw, H. H.: The Fall in Blood Pressure During Spinal Anesthesia, *Ann. Surg.* **104**:41, 1936.

11. Burch, J. C., and Harrison, T. R.: Effect of Spinal Anesthesia on Cardiac Output, *Arch. Surg.* **21**:330 (Aug.) 1930.

constriction.¹² However, that would be expected to elevate the blood pressure more than the observed 7.5 per cent. Since a flaccid paralysis of voluntary muscles occurred in all instances, the blood pressure may have been maintained either by an adequate vasoconstriction in the unanesthetized area of the body or by a partial generalized vasoconstriction in the anesthetized part of the body. In the two experiments in which there was no change in the blood pressure it may be that the vasodilatation opens up such a vast additional capillary bed through which the blood flow is distributed that, in spite of an adequate blood pressure, the volume of flow through any one channel is diminished. Since the tissue metabolism is not hindered as in ether anesthesia,¹³ the oxygen is removed in a greater than normal quantity during this paradoxical stasis. This may not be in accord with the finding of an elevated oxygen content of the venous blood in sympathectomized animals.¹⁴ However, in these animals there had been time for some compensation from the acute vasodilatation, and normal muscular tone and function were present to aid in the movement of blood toward the heart.

3. An increase in the arteriovenous difference. This is the consequence of the lowered oxygen content of the venous blood.

4. Stagnant anoxia. The findings of a perfectly saturated arterial blood and a lowered oxygen content of the venous blood, or an increased arteriovenous difference, are typical of a stagnant anoxia.¹⁵ The stagnant anoxia of spinal anesthesia differs from the anoxic anoxia of ether anesthesia in that the blood oxygen reaches the tissues at an adequate available tension but in an insufficient quantity for the requirements of the tissue metabolism. The results indicate that the stagnant anoxia is general and will vary in degree with the extent of the area anesthetized or the magnitude of the vasoconstrictor paralysis and vasomotor compensation. The significance of anoxia in surgical anesthesia has been discussed in a previous communication.¹

SUMMARY

Spinal anesthesia in dogs causes the following changes: (1) an increase in the oxygen saturation of the arterial blood, a decrease in

12. Freeman, N. E.: *Hemorrhage in Relation to Shock: Experimental Effect of Intravenous Injections of Saline, Gum Acacia, and Blood on the Rate of Adrenal Secretion Resulting from Hemorrhage*, *Ann. Surg.* **101**:484, 1935. Aub and Cunningham.⁶

13. Brow, G. R., and Long, C. N. H.: *Biochemical Changes in the Heart During Anesthesia*, *Anesth. & Analg.* **9**:193, 1930.

14. Freeman, N. E.: Personal communication to the authors.

15. Barcroft, J.: *Anoxaemia*, *Lancet* **2**:485 (Sept. 4) 1920.

the oxygen content and saturation of the venous blood, and an increase in the arteriovenous oxygen difference and (2) pale, blanched-appearing lungs, possibly indicating incompletely filled lung capillaries.

CONCLUSION

The foregoing changes indicate the existence of a stagnant anoxia. It is suggested that the anoxia may be minimized by the use of small doses of the anesthetizing drug or by controlling the administration in such a way as to involve a minimum number of the sympathetic vasoconstrictor fibers and employing vasoconstricting drugs which act principally on the capillary walls.

EXPERIMENTAL CEREBRAL TRAUMA

THE FLUID CONTENT OF THE BRAIN AFTER TRAUMA TO THE HEAD

COBB PILCHER, M.D.

NASHVILLE, TENN.

On no subject is there greater divergence of opinion than on the proper methods of treatment of injuries of the head with their resultant cerebral damage. Fay¹ advocated an extreme degree of dehydration by the use of hypertonic solutions, both intravenously and by bowel, and rigid restriction of the fluid intake; Munro² advised reduction of pressure and removal of blood by frequent spinal punctures; Sachs³ expressed the opinion that spinal puncture is dangerous and contra-indicated, and Dandy⁴ advised against the use of both hypertonic solutions and spinal puncture, preferring operative decompression in cases in which there is evidence of a high increase in the intracranial pressure.

The reason for the contradictory nature of these opinions is not difficult to find. It is based on ignorance of the mechanism of the cerebral damage attending injuries of the head. The literature abounds with postmortem statistics and clinical opinions which attribute the cause of symptoms following injuries to the head to petechial hemorrhage, molecular displacement, edema (both local and general), "traumatic hydrocephalus" and other hypothetic disorders. But there is little positive proof of the existence of any of them.

Adequate experimental studies on the subject are meager. In 1894 Halliburton⁵ first called attention to the physiologic significance of the

From the Department of Surgery, Vanderbilt University School of Medicine.

1. Fay, T.: Head Injuries: Result Obtained with Dehydration in Forty-Eight Consecutive Cases, *J. Iowa M. Soc.* **20**:447, 1930; Generalized Pressure Atrophy of the Brain, Secondary to Traumatic and Pathologic Involvement of Pacchionian Bodies, *J. A. M. A.* **94**:245 (Jan. 25) 1930; The Treatment of Acute and Chronic Cases of Cerebral Trauma, by Methods of Dehydration, *Ann. Surg.* **101**:76, 1935.

2. Munro, D.: The Diagnosis, Treatment and Immediate Prognosis of Cerebral Trauma: An Introductory Study of 1,494 Cases, *New England J. Med.* **210**:287 (Feb. 8) 1934; The Therapeutic Value of Lumbar Puncture in the Treatment of Cranial and Intracranial Injury, *Boston M. & S. J.* **193**:1187 (Dec. 24) 1925.

3. Sachs, E.: The Diagnosis and Treatment of Head Injuries, *J. A. M. A.* **81**:2159 (Dec. 29) 1923; Head Injuries, *Internat. J. Med. & Surg.* **46**:567, 1933.

4. Dandy, W. E.: Diagnosis and Treatment of Injuries of the Head, *J. A. M. A.* **101**:772 (Sept. 2) 1933.

5. Halliburton, W. D.: The Proteids of the Nervous System, *J. Physiol.* **15**:90, 1894.

fluid content of the brain and pointed out the marked difference between the gray and the white matter in this respect. His findings and conclusions were reiterated in a later paper.⁶ In studies on the brains of men, monkeys, dogs and cats he found the average fluid content of the normal gray matter to be 83.5 per cent, and that of the white matter, 69.9 per cent. In 1896 there appeared a monograph by Leonard Hill on "The Cerebral Circulation,"⁷ in which he identified cerebral edema as fluid squeezed out of capillaries by some already existing cerebral compression. Shortly thereafter, Courtney⁸ suggested that a vasomotor paralysis resulting from the original injury to the head gave rise to arteriolar dilatation and subsequently to edema. In 1901 Cannon⁹ summarized existing opinions and reported experiments on trauma to the head, adding hypothetical anemia and osmotic changes to the possible causes of cerebral edema. Liesegang and Mayr¹⁰ in 1912 attributed cerebral edema to accumulation of acid resulting from anemia of the brain.

In these early papers and in nearly all subsequent studies edema of the brain has been assumed to be the principal compressing factor in those cases of injury to the head in which there was no gross hemorrhage or major bony depressions. Some authors, particularly in France and Germany, have postulated the existence of local edema about the third ventricle (Arnaud¹¹), the aqueduct (Denis,¹² Karitzky¹³) or the outlet of the fourth ventricle (Hauptmann¹⁴), with a resulting obstructive hydrocephalus.

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Most of the meager experimental studies on the subject of cerebral edema are subject to various criticisms. Apfelmach¹⁵ determined the fluid content of blocks of traumatized brains removed at autopsy but apparently did not separate the gray from the white matter or determine the proportions of each in the blocks. Since the gray and the white matter may differ 10 per cent or more in their water contents, Apfelmach's values cannot be considered significant. The same objection applies to studies on heat stroke by McKenzie and LeCount,¹⁶ as does also the objection that the studies were made at varying and often long intervals after death. The dogs' brains studied by Masserman and Schaller¹⁷ were dried only twenty-four hours at an unstated temperature. Histologic evidence of edema of the brain (Winkelman and Eckel,¹⁸ Masserman and Schaller,¹⁷ Rand and Courville¹⁹ and Hoff²⁰) cannot be considered conclusive on account of the many variable factors in the preparation of the material, such as fixation, dehydration, cutting and staining.

There have been no direct experimental studies on the fluid contents of traumatized brains. This fact, as well as many other shortcomings in existing knowledge of the mechanism of injuries to the head, has been recently emphasized in the comprehensive and critically written review of Lehman and Parker.²¹ The reader is referred to this paper and to those of Masserman²² and Winkelman and Eckel¹⁸ for detailed bibliographies.

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22. Masserman, J. H.: Intracranial Hydrodynamics: Central Nervous System: Shock and Edema Following Rapid Fluid Decompression of the Ventriculosubarachnoid Spaces, *J. Nerv. & Ment. Dis.* **80**:138, 1934; Cerebrospinal Hydrodynamics: IV. Clinical Experimental Studies, *Arch. Neurol. & Psychiat.* **32**:523 (Sept.) 1934. Masserman and Schaller.¹⁷

The experiments to be reported herein were designed to determine the effect of trauma to the head on the fluid content of various portions of the brain and on the volume outflow of cerebrospinal fluid. In other experiments the effect of the intravenous administration of hypertonic solution of dextrose in traumatized animals was determined.

METHODS AND RESULTS

All of the sixty experiments were performed on dogs weighing from 7 to 12 Kg. The animals were anesthetized with sodium barbital, 0.3 Gm. per kilogram of body weight, administered intravenously at least two hours before the beginning of the experiments. The animal's head was held rigidly in a constant position throughout the experiment. Cerebrospinal fluid pressure was determined by means of a needle in the cisterna magna connected with a water manometer. Arterial blood pressure was recorded by means of a cannula in the femoral artery.

Measured trauma was administered to the head by dropping a standard 500 or 1,000 Gm. metal weight on the vertex of the head from a constant height of 60 inches (154 cm.). In each experiment the weight was dropped twice in rapid succession.

After the conclusion of one of the various types of procedure to be described, each experiment was terminated by stabbing the heart. The brain was immediately removed (requiring seven minutes or less), and specimens of gray and of white matter from the cerebral cortex and of gray matter from the cerebellum and a portion of the medulla and pons were quickly separated, placed in weighing bottles or beakers and weighed. Gray matter and white matter were separated by a standard rapid technic, by means of which a minimum of one type of tissue was left clinging to the specimen of the other. A sharp knife was used, and great care was exercised to avoid compressing or macerating the specimens. The constancy of the findings to be related attests the accuracy of the separation.

Specimens were dried to constant weight in an oven at 60 C. (usually requiring four or five days), and their fluid and solid contents were thus determined.

Some animals showed extravasation of blood into the scalp or temporal muscle, and an occasional small laceration of the scalp was produced, but in no instance was either fracture of the skull or perceptible intracranial hemorrhage produced by the trauma. One animal died five minutes after the trauma without showing elevation of the cerebrospinal fluid pressure or of the blood pressure. In this dog the fluid contents of the several specimens from the brain were within the normal range. The results of this experiment are not included in the tables.

In the normal dog, with the head in the position used throughout these experiments, the cerebrospinal fluid usually rose to the top of the needle and occasionally dripped out slowly. It did not rise sufficiently high to become visible in the manometer, to which the needle was attached by an adapter and a short rubber tube. The distance from the needle to the zero point of the manometer was 2 cm. The pressure was considered normal when the fluid was not visible in the manometer, and this normal pressure is designated in the tables by the symbol \pm . This degree of pressure (\pm) was observed in all animals before the infliction of the trauma.

The various types of experiments will be considered separately, and average findings in all groups of dogs will later appear in the composite table 7.

GROUP 1.—*Normal Controls.*—Five dogs were killed twelve hours after receiving the usual dose of barbital and being kept in the same position as the animals in the remaining experiments. Table 1 shows the fluid contents of the portions of their brains examined. The relatively narrow limits of variation are clearly shown. The values found correspond closely to those found by Calhoun and myself²³ by the same method in twenty-four laboratory dogs which had been previously used for various experiments not involving the nervous system. In

TABLE 1.—*Percentage of Water in the Brains of Normal Dogs Anesthetized with Sodium Barbital*

Dog No.	Fluid in Cerebral Gray Matter, %	Fluid in Cerebral White Matter, %	Fluid in Cerebellar Gray Matter, %	Fluid in Medulla Oblongata, %
T7.....	79.9	68.8	79.8	70.4
T14.....	79.8	67.0	80.0	70.2
T24.....	79.2	68.2	79.6	70.8
T44.....	78.3	68.8	79.7	71.9
T45.....	79.8	67.4	79.2	71.1
Averages.....	79.4	68.0	79.6	70.9

TABLE 2.—*Fluid Content of the Brains of Dogs Killed at Arbitrary Intervals After Trauma by a 500 Gm. Weight*

Dog No.	Time Dog Was Killed, Hours After Trauma	Immediate Rise in Mean Blood Pressure, Mm. of Hg	Later Rise in Mean Blood Pressure, Mm. of Hg	Cerebrospinal Fluid Pressure		Fluid in Cerebral Gray Matter, %	Fluid in Cerebral White Matter, %	Fluid in Cerebellar Gray Matter, %	Fluid in Medulla Oblongata, %
				Maximum Increase, Mm. of H ₂ O	Increase at End of Experiment, Mm. of H ₂ O				
T1	2	0	0	±	±	82.3	71.0	82.2	74.0
T2	2	5	20	30	30	79.8	69.5	80.5	70.0
T3	2	10	0	20	20	79.5	67.8	80.1	70.0
T4	2	8	0	±	±	79.7	66.0	80.1	69.3
T5	2	0	0	±	±	79.3	68.5	80.3	71.6
T6	4	3	10	35	35	81.0	68.8	80.7	71.2
T51	4	6	10	30	±	79.4	68.2	80.5	70.1
T8	8	0	14	40	±	80.8	70.6	81.2	71.8
T9	8	0	8	20	10	80.1	70.4	80.9	70.2
T10	24	0	0	10	±	79.7	69.5	80.5	70.5
T54	24	0	10	25	5	79.9	69.8	80.4	70.6
T56	24	4	16	35	20	79.5	69.6	80.2	70.2
Average.....						80.1	69.1	80.6	70.8

three of these animals the cerebrospinal fluid pressure was observed throughout the experiments and was never found to rise above the normal level. Similarly, the mean blood pressure maintained a rather constant level, tending to fall slightly after about eight hours.

GROUP 2.—*Trauma by a 500 Gm. Weight; Animals Killed After Various Intervals.*—Five of the animals in this group were killed two hours after trauma, and two were killed four hours, two eight hours and three twenty-four hours after trauma. The results are shown in table 2.

23. Pilcher, C., and Calhoun, J. A.: Unpublished observations.

An increase in the cerebrospinal fluid pressure within two hours was produced in only two of the five dogs, and the increase in pressure did not exceed 40 mm. of water in any of the twelve animals. A typical curve of cerebrospinal fluid pressure after this degree of trauma is shown in chart 1.

Changes in blood pressure were not marked in any animals of this group.

The fluid content of the various portions of the brain showed small variations in individual instances, but the average values indicate a small but definite increase in the fluid content of the cerebral and the cerebellar gray matter, beginning two hours after the trauma and increasing until the eight hour period, followed by a return close to the average normal level at the end of twenty-four hours. On the other hand, the average fluid content of the white matter and the medulla did not show a significant increase until eight hours after trauma. This increase persisted for twenty-four hours in the cerebral white matter but not in the medulla. The average increases observed in the fluid content were very small, the greatest alteration being an average increase of 1.5 per cent in the cerebral white matter after eight hours. The possible significance of changes of this low order of magnitude will be discussed later.

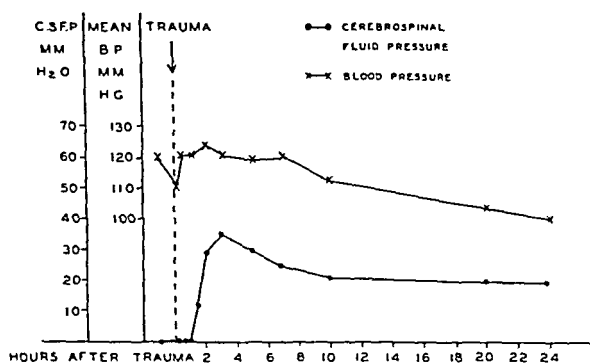


Chart 1 (dog T 56).—Effect of a 500 Gm. weight.

GROUP 3.—*Trauma by a 1,000 Gm. Weight; Animals Killed After Six Hours.*—The animals in group 2 exhibited an inconstant and not marked increase in intracranial pressure. The greatest change in the water content of their brains was found in those killed four or eight hours after trauma. Therefore, in the four dogs of group 3 the degree of trauma was doubled, and the animals were killed six hours after trauma. The results are shown in table 3.

The cerebrospinal fluid pressure was markedly elevated in three animals and moderately elevated in one, and these changes persisted without significant alteration until the termination of the experiments. The mean blood pressure showed some elevation in three of the four animals.

The average fluid contents of the various parts of the brain closely approximated or were slightly lower than the normal values in group 1, except in the cerebral gray matter, where the fluid content was slightly greater than the average normal in three of the four animals.

GROUP 4.—*Trauma by a 1,000 Gm. Weight; Animals Killed at the Time of the Maximum Increase in Cerebrospinal Fluid Pressure.*—Table 4 shows the results in this group of ten dogs. A marked increase in the cerebrospinal fluid

The fluid contents were again almost unexceptionally constant. The average values were not only slightly greater than the control levels but also exceeded slightly the average fluid contents observed in groups 4 and 5. In fact, the values in this group were higher than in any other group except group 2C (table 7).

TABLE 5.—*Fluid Content of the Brains of Dogs Killed Immediately After Receiving 50 Cc. of 50 per Cent Solution of Dextrose Intravenously; Previous Trauma by a 1,000 Gm. Weight*

Dog No.	Interval Between Trauma and Injection of Dextrose, Hr.	Immediate Rise in Mean Blood Pressure, Mm. of Hg	Later Rise in Mean Blood Pressure, Mm. of Hg	Cerebrospinal Fluid Pressure		Fluid in Cerebral Gray Matter, %	Fluid in Cerebral White Matter, %	Fluid in Cerebellar Gray Matter, %	Fluid in Medulla Oblongata, %
				Maximum Increase Before Injection, Mm. of H ₂ O	Increase at Time of Killing, Mm. of H ₂ O				
T27	3½	20	9	140	±	80.2	69.5	79.6	73.8
T28	3	22	10	130	±	79.6	70.2	79.4	70.8
T29	7½	24	0	80	±	80.0	69.5	81.0	72.3
T30	4	69	0	200	±	80.8	68.9	79.7	72.3
T33	3½	13	0	110	±	79.2	66.6	78.2	80.0
Average.....						79.9	68.9	79.6	71.8

TABLE 6.—*Fluid Content of the Brains of Dogs Killed Two Hours After Receiving 50 Cc. of 50 per Cent Solution of Dextrose Intravenously; Previous Trauma by a 1,000 Gm. Weight*

Dog No.	Interval Between Trauma and Injection of Dextrose, Hr.	Immediate Rise in Mean Blood Pressure, Mm. of Hg	Later Rise in Mean Blood Pressure, Mm. of Hg	Cerebrospinal Fluid Pressure		Fluid in Cerebral Gray Matter, %	Fluid in Cerebral White Matter, %	Fluid in Cerebellar Gray Matter, %	Fluid in Medulla Oblongata, %
				Maximum Increase Before Injection, Mm. of H ₂ O	Increase at Time of Killing, Mm. of H ₂ O				
T32	7¼	27	0	65	10	81.2	70.4	80.3	72.0
T34	4	0	0	70	50	80.4	69.4	80.4	71.2
T35	3½	3	6	140	80	79.8	68.4	80.5	73.6
T36	5	8	0	40	65	81.0	68.0	80.6	71.7
T37	3	15	0	104	±	79.7	69.1	80.1	70.5
Average.....						80.4	69.1	80.4	71.8

GROUP 7.—*Lumbar Cerebrospinal Fluid Outflow in Untraumatized Dogs.*—In two dogs the outflow of cerebrospinal fluid from an 18 gage needle (the same needle was used in both experiments and in all experiments in group 8), measured in drops per minute, was determined over a period of twenty-four hours. The needle was inserted into the lumbar subarachnoid space with the animal's head in the holder, as in the preceding experiments, but with the body twisted to lie on its side. The needle was left open at all times.

During the first hour after lumbar puncture the outflow varied greatly from minute to minute, usually with a marked respiratory fluctuation. After this period

of initial variation, the flow gradually assumed a relatively constant rate of one drop in one and one half to two minutes, and this rate was maintained throughout the twenty-four hours of observation.

GROUP 8.—Effect of Trauma by a 1,000 Gm. Weight on the Lumbar Outflow of Cerebrospinal Fluid.—The outflow was determined as in group 7, and the same initial fluctuation was observed in all of the six animals. However, a much slower control rate of flow was observed in three of the animals than in the two dogs of group 7. Trauma was administered two hours after lumbar puncture, when the outflow had assumed a constant rate.

The results observed were not consistent or conclusive (table 8). A variable and unsustained increase in flow usually occurred immediately after trauma. At later periods the rate of flow was relatively unchanged in three animals (T 39,

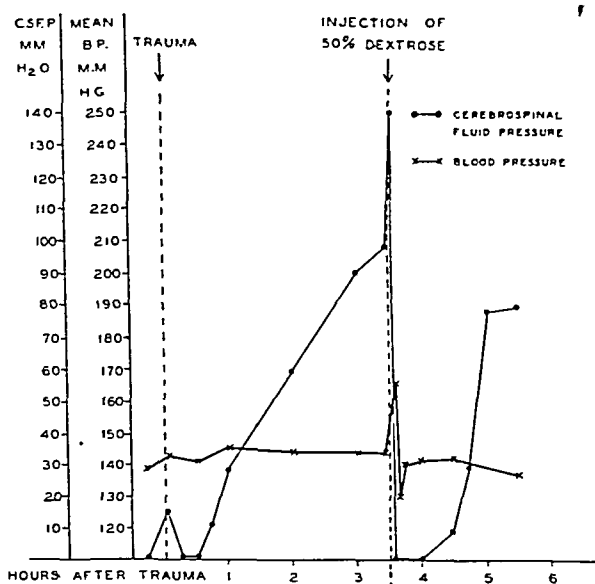


Chart 3 (dog T 35).—Effect of a 1,000 Gm. weight. Fifty cubic centimeters of 50 per cent solution of dextrose was injected three and one-half hours after trauma.

T 40 and T 46), seemed to be definitely slowed in one (T 43) and showed some degree of sustained increase in two (T 42 and T 47).

GROUP 9.—Effect on Cerebrospinal Fluid Pressure of the Intracisternal Injection of Small Quantities of Physiologic Solution of Sodium Chloride.—Before evaluating the significance of the small changes observed in the fluid content of the brain, it seemed essential to determine whether such small increases in the fluid content could be responsible for the rise observed in the cerebrospinal fluid pressure. Three dogs were used for this purpose. A three way stopcock was interpolated between the cisternal needle and the manometer, in order that fluid might be withdrawn or injected with only a momentary break in the pressure measurements.

After a normal constant cerebrospinal fluid pressure had been observed for one hour, a volume of physiologic solution of sodium chloride estimated to be equivalent to 0.5 per cent of the weight of the dog's brain was injected into the cisterna magna, and the stopcock was immediately turned back to reestablish communication between the cistern and the manometer. After the cerebrospinal fluid pressure was observed, the stopcock was opened to allow the escape of fluid

TABLE 7.—Average Fluid Contents of the Brains in the Various Groups of Experiments

Type of Experiment	Number of Experiments	Fluid in Cerebral Gray Matter, %	Fluid in Cerebral White Matter, %	Fluid in Cerebellar Gray Matter, %	Fluid in Medulla Oblongata, %
1. Normal controls	5	79.4	68.0	79.6	70.9
2a. Brain removed 2 hours after trauma by 500 Gm. weight.....	5	80.1	68.6	80.6	70.9
2b. Brain removed 4 hours after trauma by 500 Gm. weight.....	2	80.2	68.5	80.6	70.7
2c. Brain removed 8 hours after trauma by 500 Gm. weight.....	2	80.4	70.5	81.0	71.0
2d. Brain removed 24 hours after trauma by 500 Gm. weight.....	3	79.7	69.6	80.4	70.4
2. Average of 2a, 2b, 2c and 2d.....	11	80.1	69.1	80.6	70.8
3. Brain removed 6 hours after trauma by 1,000 Gm. weight.....	4	80.3	67.8	79.9	68.9
4. Brain removed at time of maximum cerebrospinal fluid pressure after trauma by 1,000 Gm. weight.....	10	80.0	68.9	79.8	70.4
5. Brain removed immediately after post-traumatic treatment with 50 per cent solution of dextrose.....	5	79.9	68.9	79.6	71.8
6. Brain removed 2 hours after posttraumatic treatment with 50 per cent solution of dextrose.....	5	80.4	69.1	80.4	71.8

TABLE 8.—Outflow of Cerebrospinal Fluid Through a Lumbar Puncture Needle After Trauma by a 1,000 Gm. Weight

Dog No.	Initial Rate, Drops per Minute	Immediately After Trauma, Drops per Minute	1 Hour After Trauma, Drops per Minute	2 Hours After Trauma, Drops per Minute	4 Hours After Trauma, Drops per Minute	24 Hours After Trauma, Drops per Minute
T39	1	3	1	1	1	3/4
T40	1/2	2	1	1/2	1/2	1/3
T42	1/6	11	1/3	1/2	1	—
T43	1/7	3/4	1/5	1/5	1/25	0
T46	1/2	2	1/2	1/3	0	—
T47	1/5	1/5	1/3	1/2	3/4	0

until the pressure had been reduced to the normal level. The entire procedure was then repeated. In this way, several readings were obtained on each animal. Subsequently, twice the volume of saline solution originally employed was injected and pressure readings made as before, and finally the volume was again doubled to obtain another series of readings. These approximate volumes were employed because most of the average increases observed in the fluid content of the brain after trauma did not exceed 1 per cent. After the readings were completed, the brain was removed, free fluid blotted away and the brain weighed.

The results are shown in table 9. Only immediate pressure readings are included, since it was the purpose of these experiments to determine only the

effects of the actual increases in the volume of the intracranial contents brought about by the injections. After injection of an amount of fluid equivalent to approximately 0.5 per cent of the weight of the brain, a definite but relatively slight rise in the cerebrospinal fluid pressure was observed, the greatest increase being 15 mm.

When a volume equivalent to approximately 1 per cent of the weight of the brain was injected, a greater increase in pressure was observed, the greatest being 60 mm. and the average 31 mm. This degree of rise in pressure is comparable to that found in some of the animals subjected to mild trauma (table 2) but does not approach that usually observed after more severe trauma (tables 3, 4, 5 and 6).

TABLE 9.—*Effect on Cerebrospinal Fluid Pressure of the Intracisternal Injection of Small Volumes of Physiologic Solution of Sodium Chloride*

Dog No.	Body Weight, Kg.	Weight of Brain, Gm.	Volume of Saline Solution Injected, Cc.	Percentage of Weight of Brain of Saline Solution Injected	Immediate Increase in Cerebrospinal Fluid Pressure, Mm. of H ₂ O	Increase in Cerebrospinal Fluid Pressure After 15 Sec.
T58	11.47	76	0.35	0.46	20	15
			0.35	0.46	15	10
			0.70	0.92	60	30
			0.70	0.92	55	40
			1.40	1.84	300	260
			1.40	1.84	450	230
T59	12.0	73	0.35	0.45	10	5
			0.35	0.45	5	±
			0.70	0.96	20	15
			0.70	0.96	10	5
			0.70	0.96	10	±
			1.40	1.92	120	100
			1.40	1.92	160	140
			0.70	0.96	15	10
T60	10.4	62	0.3	0.45	5	±
			0.3	0.45	10	5
			0.6	0.97	25	15
			0.6	0.97	40	25
			0.6	0.97	30	20
			1.2	1.94	205	150
			1.2	1.94	165	120

Injection of amounts of fluid equivalent to approximately 2 per cent of the weight of the brain produced an immediate marked increase in the cerebrospinal fluid pressure. This degree of increase was greater than that usually observed after severe trauma.

COMMENT

Before arriving at conclusions from the experiments reported herein, it is necessary to consider the several essential limitations inherent in the method of study.

It is impossible to determine the fluid content of the brain both before and after trauma in the same animal. Therefore, the only available basis for comparison consists of average findings in normal animals. This objection is obviated to some extent by the small degree of variation observed in the normal animals.

Similarly, in the experimental animals, in spite of occasional individual variations, the great majority of the individual findings did not vary significantly from the average of their groups.

After careful study of the tables, it seems justifiable to conclude that any change in average findings as great as 1 per cent of fluid content may be considered as beyond the probable limits of error of the method.

If the validity of the results is accepted within these limits, it is next in importance to recognize what degree of increase in the total intracranial contents is necessary to produce a significant increase in the cerebrospinal fluid pressure. The results of the experiments on the animals in group 9 (table 9) indicate a marked increase in the degree of rise in pressure resulting from increasing the intracranial contents more than the equivalent of 1 per cent of the weight of the brain. In other words, 1 per cent of the weight of the brain may be considered as the limit beyond which the quantity of intracranial contents cannot be increased without producing a marked rise in pressure. It is apparent that an increase in the tissue fluid comparable to that found in edematous tissues elsewhere in the body (from 2 to 6 per cent in tissue as dense as muscle²⁴) could exist in the brain only if the remaining intracranial contents (i. e., blood and cerebrospinal fluid) were greatly diminished.

The rise in cerebrospinal fluid pressure observed in these experiments could conceivably arise from an increase in tissue fluids, in cerebrospinal fluid or in intracranial blood volume or from any combinations of alterations in their respective volumes which resulted in an increase in the total intracranial fluid volume.

A survey of the composite average results shown in table 7 shows at once that no great change in tissue fluids has resulted from trauma to the head in these experiments. In only two groups (2 and 6) were as many as two of the four types of brain tissue examined found to have as much as 1 per cent greater fluid content than was found in the average normal animal. On account of the striking uniformity of the results, it may be justifiable to conclude that a small increase in fluid content (particularly of the gray matter) probably follows trauma to the head. But the degree of increase observed

24. Pilcher, C.; Calhoun, J. A.; Cullen, G. E., and Harrison, T. R.: Studies in Congestive Heart Failure: V. The Potassium Content of Skeletal Muscle Obtained by Biopsy, *J. Clin. Investigation* 9:191, 1930. Harrison, T. R.; Pilcher, C., and Ewing, G.: Studies in Congestive Heart Failure: IV. The Potassium Content of Skeletal and Cardiac Muscle, *ibid.* 8:325, 1930.

was not in proportion to and probably should not be considered as the sole cause of the increase in cerebrospinal fluid pressure which occurred.

The results of the experiments on the cerebrospinal fluid outflow, as stated previously, were not consistent or conclusive (table 8). From them it may be said only that the outflow of cerebrospinal fluid is increased in volume in some cases after trauma to the head, but this may not necessarily be an index of the production of cerebrospinal fluid, since the outflow would probably be increased by any alteration in intracranial contents producing increased pressure. Of interest in this connection are the findings of Hoff,²⁰ who injected fluorescein intravenously in estimating the production of cerebrospinal fluid and found an increase after measured trauma to the head. Recent experiments by Parker and Lehman²⁵ have demonstrated that a rise in the cerebrospinal fluid pressure occurs after replacement of small amounts of cerebrospinal fluid with equal volumes of blood serum, defibrinated blood or solution of hemoglobin but not after replacement with washed red blood cells. The authors concluded: "It is probable that the phenomena reported are the result of the increase of osmotic pressure of the cerebrospinal fluid due to the introduction of blood proteins."

The results of experiments on the effect of hypertonic solution of dextrose (table 5 and 6) confirm, for the first time in traumatized animals, the original observations of Weed and McKibben,²⁶ Weed and Hughson²⁷ and many later investigators on the reduction of cerebrospinal fluid pressure after the intravenous administration of these solutions. Further, they are not incompatible with the alterations in the bulk of the brain found by Weed and McKibben²⁸ after intravenous injections of solutions of various concentrations, for these alterations may well have been due to changes in such factors as ventricular size or intracerebral blood volume.

The results of the experiments reported herein also confirm the findings of Masserman,²⁹ who measured the cerebrospinal fluid pressure

25. Parker, W. P., and Lehman, E. P.: Personal communication to the author.

26. Weed, L. H., and McKibben, P. S.: Pressure Changes in the Cerebrospinal Fluid Following Intravenous Injection of Solutions of Various Concentrations, *Am. J. Physiol.* **48**:512, 1919.

27. Weed, L. H., and Hughson, W.: Systemic Effects of the Intravenous Injection of Solutions of Various Concentrations, with Especial Reference to the Cerebrospinal Fluid, *Am. J. Physiol.* **58**:53, 1921.

28. Weed, L. H., and McKibben, P. S.: Experimental Alteration of Brain Bulk, *Am. J. Physiol.* **48**:531, 1919.

29. Masserman, J. H.: Effects of Intravenous Administration of Hypertonic Solutions of Dextrose, with Special Reference to the Cerebrospinal Fluid Pressure, *J. A. M. A.* **102**:2084 (June 23) 1934.

in untraumatized human subjects receiving intravenous injections of hypertonic solutions. He observed an original fall in pressure followed by a rise to a level equal to or greater than the control value. The present experiments suggest that in traumatized dogs concomitant with this secondary rise in pressure, there may be an increase in the cerebral tissue fluid greater than that present before the injection. These findings cast considerable doubt on the wisdom of the intravenous use of hypertonic solutions in the treatment of injuries of the head.

Regarding intracranial blood volume, there is little evidence. Wolff and Blumgart³⁰ found a decrease in the velocity of blood flow through the brain after increasing the cerebrospinal fluid pressure through a needle in the cisterna magna. However, they believed that "through cerebral vasodilatation, the flow, though slowed, is increased in volume . . ." Pilcher,³¹ using the arteriovenous oxygen difference method, found a decrease in the volume flow of blood through the brain after the intravenous injection of hypertonic solutions in normal dogs. The only observations on the actual intracerebral blood volume are those of Weil, Zeiss and Cleveland,³² who injected colloidal silver intravenously and determined the silver content of the brain (which does not remove colloidal silver from the blood). They found an increase in the blood volume of the brain immediately (from five to fifteen minutes) after the intravenous injection of 15 per cent sodium chloride. There are no recorded observations pertaining to intracranial blood volume after cerebral trauma. It seems probable that this may be an important factor in the mechanism producing the increased cerebrospinal fluid pressure which follows trauma to the head.

SUMMARY AND CONCLUSIONS

The fluid content of various portions of the dog's brain has been determined after measured trauma of varying degrees.

After trauma sufficient to produce a definite elevation in the cerebrospinal fluid pressure, the fluid content of the brain was slightly, if at all, increased above the average normal level. The small average

30. Wolff, H. G., and Blumgart, H. L.: The Cerebral Circulation: VI. The Effect of Normal and Increased Intracranial Cerebrospinal Fluid Pressure on the Velocity of Intracranial Blood Flow, *Arch. Neurol. & Psychiat.* **21**:795 (April) 1929.

31. Pilcher, C.: Cerebral Blood Flow: I. The Effect of Intravenous Administration of Hypertonic and Hypotonic Solutions on the Volume Flow of Blood Through the Brain, *Arch. Neurol. & Psychiat.* **24**:899 (Nov.) 1930.

32. Weil, A.; Zeiss, F. R., and Cleveland, D. A.: The Determination of the Amount of Blood in the Central Nervous System After Injection of Hypertonic Solutions, *Am. J. Physiol.* **98**:363, 1931.

increase observed is not believed to be sufficiently great to account for the elevation of the cerebrospinal fluid pressure.

There is no conclusive evidence in these studies, or in those of other authors, indicating the existence of marked posttraumatic cerebral edema.

The outflow of lumbar cerebrospinal fluid after trauma to the head was not consistently altered but in some instances showed a sustained increase.

It seems probable that other factors, such as cerebrospinal fluid volume and intracranial blood volume, are of greater importance than cerebral edema in producing the increased intracranial pressure which follows trauma to the head.

DISLOCATION AND FRACTURE-DISLOCATION OF LOWER CERVICAL VERTEBRAE

JAMES PIERCE COLE, M.D.*

NEW YORK

Nearly as far back as one is able to peruse the annals of medical history one finds references to fractures and fracture-dislocations of the cervical portion of the spine. An injury involving this segment of the spine rightly struck terror into the heart of the surgeon who was called on to treat it. About 2500 B. C. the timidity of a surgeon regarding such an injury was recorded in a papyrus written during that period, in which it was stated:¹ "One having a crushed vertebra in his neck, he is unconscious of his two arms and his two legs, and he is speechless. An ailment not to be treated." The reluctance to treat such a lesion can only be surmised.

Hippocrates² formed a rational and sound plan for the treatment of a lesion of this type in the acute stage. His method consisted in extension of the head with the patient in a recumbent position. Despite his teachings his contemporaries were prone to practice a form of therapy called succussion. The unfortunate patient was placed on a vertical ladder with the head down. The ladder was then shaken forcefully in the hope that reposition of the involved vertebra might take place. Needless to say, the torture experienced by the patient was terrific, and the mortality rate was high. The father of medicine decried such a brutal manner of treatment but his laments were of no avail at that time. It is to him, however, that the modern nonoperative form of treatment for such a lesion owes its origin, although various physicians have introduced minor modifications of his principle.

Guy de Chauliac³ and others who dominated the surgical world about the fifth century used much the same method of treatment as

* An Annie C. Kane Fellow.

From the New York Orthopaedic Dispensary and Hospital.

Thesis presented in partial fulfilment of the requirements for the degree of Doctor of Medical Science, Columbia University.

1. Breasted, James H.: *The Edwin Smith Surgical Papyrus*, Chicago, University of Chicago Press, 1930.

2. *The Genuine Works of Hippocrates*, translated by Francis Adams, New York, William Wood & Company, 1929.

3. de Chauliac, Guy: *On Wounds and Fractures*, translated by W. A. Brennan, Chicago, W. A. Brennan, 1923.

Hippocrates. Paré,⁴ who contributed greatly to the knowledge of traumatic lesions, obtained many good results by traction exerted on the extended head.

Skepticism as to the wisdom of attempting reduction of a fracture of a cervical vertebra was universal during the early part of the nineteenth century. Boyer⁵ said: "Any attempt at setting these fractures would not only be useless but dangerous, by the straining it would occasion." Cupping and scarification of the cervical region, as well as the use of setons and ointments, were recommended by him, and these appear to have been the only armamentarium resorted to by the surgeons of his day.

Chelius⁶ admitted that the patient with such a fracture might be left alone. He said that the pain would gradually subside and that the patient would have no inconvenience other than an unnatural position of the head and restricted motion. Fearful lest the spinal cord be torn asunder by manipulation or matters be made worse, Dupuytren,⁷ and others agreed to this policy of *laissez faire*. The attitude of the medical profession in regard to lesions of this nature can be summed up in the words of Abernethy:⁸ "They are cases so generally fatal, that I am convinced an assembly of old surgeons would doubt that there was a possibility of recovery in any case." One is thankful that these teachings as regards traumatic lesions of the cervical portion of the spine in the acute stages have been discarded.

In 1814 Henry Cline performed what is now known as laminectomy for the removal of pressing vertebral arches. His operation was designed primarily for the treatment of fracture of the spine, but at that time the operation was met with a storm of criticism. A strong controversy arose between Sir Astley Cooper⁹ and Sir Charles Bell as to the value and propriety of resection of the vertebral arches. As a result of this operation, as well as of the controversy which arose, the medical profession was shaken from the doldrums of thought in regard to these lesions, and greater interest was stimulated.

4. Paré, Ambroise: *The Workes of that Famous Chirurgion Ambrose Parey*, translated by T. Johnson, London, Mary Clark, 1678.

5. Boyer, Alexis: *The Lectures of Boyer upon Diseases of the Bones*, arranged by A. Richerand and translated by M. Farrell, London, John Callow, 1807.

6. von Chelius, M. J.: *System of Surgery*, translated by John F. South, London, Henry Renshaw, 1845.

7. Dupuytren, Guillaume: *On the Injuries and Diseases of Bones*, translated and edited by F. leGros Clark, London, Sydenham Society, 1847.

8. Abernethy, John: *Lectures on Anatomy, Surgery and Pathology*, London, James Bullock, 1828.

9. Cooper, Astley, P.: *A Treatise on Dislocations and on Fractures of the Joints*, ed. 2, London, Longman, Hurst, Rees, Orme and Browne, 1823.

Ashhurst¹⁰ in 1867 reviewed the literature on the subject. The treatise which he wrote is an admirable one, constituting a profound advancement in the knowledge of this type of lesion in regard to diagnosis and the pathologic picture. Concerning paralysis, he said:

The cause of paralysis in some cases is obscure. In fatal cases the post-mortem appearances have consisted in effusion of blood with softening of the cord structure, but in some cases which have recovered, the paralysis has been so ephemeral as to give rise to the impression that the cause has been congestion rather than actual extravasation.

In regard to diagnosis, he stated:

If paralysis below the seat of injury be immediate, complete and permanent, there is every reason to fear that the cord has been absolutely divided. If paralysis is immediate but not permanent it is probably a case of contusion of the cord without structural damage. If paralysis comes on as a late sign, increases to a certain point, then to diminish again, it is probably an effusion, within or without the cord which, under favorable circumstances, may be absorbed. If paralysis is progressive, if not arrested, it will invariably sooner or later prove fatal.

From the literature Ashhurst collected reports of 212 cases of injury to the cervical region of the spine. The mortality rate in this series was 77 per cent; 18 per cent of the patients recovered from the injury and 3 per cent were relieved. The treatment was by extension, resection or simple general care of the patient.

In 1869 Blasius¹¹ collected reports of 159 cases of definitely diagnosed dislocation of the cervical portion of the spine. In 123 of these cases the injury proved fatal, while in 36 there was improvement. In the cases of bilateral forward dislocation, the severest type, there was a mortality rate of 92.6 per cent.

These startling statistics alarmed and aroused surgeons who saw the inadequacy of the treatment for this type of lesion. A method of reduction was described by Walton¹² in 1889. This method is still in use at the present time and is called the retrolateral flexion maneuver with rotation. Walton reported 5 cases of dislocation of the cervical vertebrae in which he used this treatment. A few years later Wagner and Stolper¹³ described a method of reduction which, in the main, is similar to that of Walton.

10. Ashhurst, John, Jr.: *Injuries of the Spine*, Philadelphia, J. B. Lippincott & Co., 1867.

11. Blasius, E.: *Die traumatischen Wirbelverrenkungen*, *Vrtljschr. f. d. prakt. Heilk.* **102**:1, 1869; **103**:46, 1869; **104**:77, 1869.

12. Walton, George L.: *Dislocation of the Cervical Vertebrae*, Boston M. & S. J. **120**:277, 1889.

13. Wagner, W., and Stolper, P.: *Die Verletzungen der Wirbelsäule und des Rückenmarks*, in Billroth, T., and Luecke, G. A.: *Deutsche Chirurgie*, Stuttgart, F. Enke, 1898, no. 40, p. 385.

With the advent of the roentgen rays, one became able to evaluate each lesion. This led to a safer and saner manner of treatment and improved results.

Taylor¹⁴ in 1929 described a method of reduction by means of forceful traction exerted on the extended head. Nine persons were treated by him. After reduction had taken place, the head and neck were immobilized in a plaster helmet. He stated that immobilization was imperative until bony ankylosis had taken place between the vertebral bodies and that bony ankylosis always took place.

One year later Langworthy¹⁵ reported 30 cases of dislocation of the cervical vertebra in which treatment was given by him. Reduction was obtained by traction in cases of unilateral as well as of bilateral injury. The mortality rate in this series was 30 per cent. Diagnosis of a unilateral dislocation was made from physical examination and by the fact that the patient was cured by manipulation of the head.

The literature on fracture-dislocation of the cervical portion of the spine is voluminous; yet nearly all of the articles concern the lesion in the acute stage. Many persons with injury to the cervical portion of the spine survive the acute stage but have residual symptoms. Reports of series of cases which have been cited deal mostly with the condition in the acute stage.

Only a limited number of articles could be found which dealt with the residual effects of the more acute lesions and their treatment. De Quervain and Hoessly¹⁶ in 1917 transplanted the spine of the scapula between adjacent cervical vertebrae to produce a fusion of these in an attempt to relieve 2 patients suffering from the residual symptoms caused by an earlier fracture-dislocation. As far as the function of the neck and the relief of preoperative symptoms were concerned, the results were reported as excellent. Hibbs¹⁷ in 1922 reported a case of fracture-dislocation of the cervical portion of the spine in which fusion was employed to relieve the patient from symptoms arising from a previously treated injury of that portion of the spine. The patient was greatly benefited by this procedure. In 1930 Krida¹⁸ reported a dislocation of the fifth cervical vertebra in a patient on whom repeated attempts at

14. Taylor, Alfred: Fracture Dislocations of the Cervical Spine, *Ann Surg.* 90:321, 1929.

15. Langworthy, M.: Dislocations of the Cervical Vertebrae, *J. A. M. A.* 94: 86 (Jan. 11) 1930.

16. de Quervain, F., and Hoessly, H.: Operative Immobilization of the Spine. *Surg., Gynec. & Obst.* 24:428, 1917.

17. Hibbs, Russell A.: Fracture-Dislocation of the Spine Treated by Fusion, *Arch. Surg.* 4:598 (May) 1922.

18. Krida, Arthur: Dislocation Between Fifth and Sixth Cervical Vertebrae: Delayed Operative Reduction and Fusion, *Am. J. Surg.* 9:560, 1930.

closed reduction had been carried out, all of which were followed by redislocation. After these attempts a portion of the cervical segment of the spine was fused; the patient was relieved from symptoms as well as from the danger of redislocation.

Cases in which the patient presents the residual effects of trauma to the cervical region have been little discussed, and it is the purpose of this paper to evaluate spinal fusion and laminectomy in reference to treatment and prognosis in cases in this category.

PRESENTATION OF CASES

Between 1923 and 1933 18 patients with dislocation or fracture-dislocation of the lower cervical vertebrae were admitted to the New

TABLE 1.—*Diagnosis and Type of Operation in Series of Cases**

Case	Diagnosis	Operation
1.....	Fr.-dis. 5 C	Spinal fusion 4 C-7 C; laminectomy 4 C and 5 C
2.....	Fr.-dis. 3 C	Spinal fusion 2 C-7 C
3.....	Fr. 6 C	Spinal fusion 5 C-7 C
4.....	Fr. 5 C	Spinal fusion 4 C-6 C
5.....	Fr.-dis. 5 C	Spinal fusion 4 C-6 C
6.....	Dis. 6 C	Spinal fusion 6 C-1 D
7.....	Fr.-dis. 6 C	Spinal fusion 5 C-1 D
8.....	Dis. 4 C	Spinal fusion 2 C-5 C
9.....	Fr.-dis. 5 C	Spinal fusion 4 C-6 C
10.....	Dis. 5 C	Spinal fusion 3 C-6 C; laminectomy 3 C-6 C
11.....	Fr.-dis. 4 C	Spinal fusion 3 C-6 C; laminectomy 4 C-5 C
12.....	Fr.-dis. 5 C	Spinal fusion 5 C-7 C
13.....	Fr. dis. 6 C	Spinal fusion 5 C-7 C
14.....	Dis. 4 C	Spinal fusion 4 C-5 C; laminectomy 4 C
15.....	Dis. 5 C	Spinal fusion 4 C-6 C
16.....	Dis. 5 C	Spinal fusion 5 C-7 C
17.....	Fr.-dis. 6 C	Spinal fusion 5 C-7 C; laminectomy 5 C
18.....	Fr.-dis. 4 C	1. Spinal fusion 3 C-6 C 2. Laminectomy 4 C-5 C 3. Laminectomy 3 C-6 C; partial excision of vertebral body 5 C

* The abbreviations may be interpreted as follows: Fr.-dis. 5 C, fracture-dislocation of the fifth cervical vertebra, etc.

York Orthopaedic Dispensary and Hospital. The average age of these patients was 29, the youngest being 19 and the oldest 55. Fourteen of the patients were men, and 4 were women. With the exception of 2 patients, the original trauma had taken place some time prior to the patient's first visit to this hospital. Two patients were seen two days after the accidents which were responsible for the lesions, while 1 was seen two weeks after the original trauma. The longest interval was sixteen years, and the average interval, sixteen months. Although there are 2 patients in the series who could be designated as having fracture-dislocation of the more acute type, the entire series is regarded as presenting the residual manifestations of acute traumatism of the lower cervical segment of the spine.

The diagnosis and type of operation performed in each case are recorded in table 1.

CAUSE OF FRACTURES AND FRACTURE-DISLOCATIONS OF THE
CERVICAL PORTION OF THE SPINE

The cervical portion of the spine has a wide range of mobility, which is dependent on many factors. The ligaments are long enough to allow great mobility, and they do not check flexion before the anterior lips of the bodies are about in contact. The ligamentum nuchae, which in the pronograde mammals acts as a powerful check to flexion, is almost useless for this purpose in man because it is not so fully developed. The articular capsules of the lateral articulations are thin and redundant in the cervical portion of the spine. The capsules, by their inability to constrain the articulations from excessive motion, permit them to glide forward into a luxated state. The cervical bodies are small, separated from each other by a relatively greater amount of intervertebral substance than is found in other areas of the spine. Likewise the lateral articulations are on a more horizontal plane, not only facilitating the motion of flexion but increasing the ease of dislocation.

Mechanically the cervicodorsal junction is unstable. It is a point where the rather flexible cervical portion of the spine meets the comparatively immobile dorsal segment. Naturally, a force exerted on the flexible segment, if of sufficient strength, will cause damage to it rather than to the relatively immobile portion. Forces tend to be concentrated on the areas where fixed and movable portions of the spine meet, as at the cervicodorsal junction.

The cervical segment of the spine, being deficient in so many stabilizing factors, having a mechanical situation which renders it vulnerable and yet being called on to furnish great ranges of mobility, gains its stability at the expense of voluntary and involuntary muscular effort. By involuntary muscular effort is meant the neuromuscular mechanism which maintains the head and neck in an erect posture during the conscious state. The muscles surrounding the cervical portion of the spine are many, and collectively they are very strong. Acting under voluntary control against a given force, these muscles are capable of protecting the spine in most instances. There are times, however, when this muscular control is off guard or is not of sufficient strength, and it is during these unguarded moments that injury to the cervical segment of the spine takes place. The degree of injury which may ensue depends on the extent of the force applied, as well as on the duration of the unguarded moment.

In this series of cases it was almost uniformly found that injury to the cervical portion of the spine had been received during a moment when the spine was not protected by a sufficient amount of muscular effort, as well as when a force producing acute flexion was applied. Seven of the 18 patients gave a history of having struck the bottom

of a swimming pool while diving. As the occiput struck the unyielding bottom the oncoming weight of the trunk and legs forced the head into acute flexion. Two patients were playing football and, while in a sitting position, were struck on the back of the head by another player, thus forcing the head into acute flexion. Injuries had been received in 2 instances when patients had fallen down stairs, bending the head forward during the fall. One case was unusual in that the injury had been received when the patient fell from the height of a few feet, landing on the buttocks. Perhaps in this case injury to the cervical portion of the spine had been caused by the snapping forward of the head, an accident which sometimes occurs in such a fall. The exact manner of the injury was not stated by a few patients.

The series, although small, emphasizes that the mechanism which causes fractures and dislocations in this area of the spine is flexion.

ORIGINAL TREATMENT

The original treatment in 3 of the 18 cases was rest in bed for a few weeks. Reduction of the lesion was attempted in 4 instances by the use of traction on the head. In 1 case traction on the head was followed by the application of a head helmet. This helmet was worn for a few weeks after its application. Manipulation of the head, followed by no supportive apparatus, was the original treatment in 3 cases. In 2 cases osteopathic or chiropractic manipulations were resorted to by the patients. Three patients were not seen elsewhere before they came to this hospital, while 2 did not present any history as regards original treatment.

PREOPERATIVE STATUS OF PATIENTS

Disability was the reason for each of the patients in this series applying to the hospital for treatment. Disability from this type of lesion, whether it is in an acute or a chronic stage, is dependent chiefly on the type and extent of injury to the cord, but partly on the degree of involvement of nerve roots and partly on the extent and type of structural damage to the vertebral column with its supportive structures.

Injury to the cord at the time of primary trauma can occur as the result of concussion, contusion, edema, hematomyelia or laceration. The degree of damage to the cord with its resultant syndromes depends on the type, extent and location of any one or a combination of these. After the integrity of the cord has been affected in any of the foregoing manners, its function may return gradually and, in the milder lesions, will sometimes return to normal, the patient suffering no disability because of the lesion of the cord. As a result of irreparable damage to the cord at the primary trauma, the disability of the patient may be of any degree and of a lasting nature, despite perfect anatomic

reduction. Some of the factors which may operate in causing continued damage to the cord are abnormally luxated vertebrae, pressing vertebral arches and bodies and sclerosis of the coverings of the cord.

To diagnose the presence of involvement of the cord is usually easy. This was true in most of these cases, yet it was difficult to form a satisfactory opinion as to the nature of the pathologic process causing the dysfunction. In the presence of dysfunction of the cord it is sometimes difficult to ascertain whether the dysfunction is due to the original trauma or to latent factors.

The neurologic syndromes, indicating the evidence of involvement of the cord in these cases, will not be presented in detail, but it may be stated that 3 patients with severe syndromes were bedridden when they were first seen at this hospital. An atypical Brown-Séquard phenomenon was present in 1 of these, the lesion being at the level of the fifth cervical segment. Milder and moderate syndromes included atrophy, hemiplegia and contracture as well as other evidence of damage to the cord.

A fracture-dislocation in the cervical portion of the spine, perfectly reduced, may still produce disability in the function of the neck. Such disability may be caused by mobility at fractures of the posterior elements, arthritic productions arising from traumatized lateral articulations, scar formation from the tearing of ligaments or articular capsules and unstable vertebrae.

If unreduced, a malaligned cervical segment of the spine may also produce symptoms referable to the head and neck. These symptoms may occur as a result of the aforementioned causes, as well as from impingement of the spinous processes and laminae.

Eight patients in the series had partial rigidity of the neck associated with severe pain in the cervical region. In another instance there was severe pain in this region without any limitation of the motion of the head. Limited motion and an unnatural position of the head were complained of by 1 patient. Stiff neck, limited motion of the head of a mild degree, a grating sensation of the cervical region and a moderate ache in the posterior cervical region were complained of by many patients. All of these symptoms were indicative of a pathologic process of the ligamentous and bony structure of the spine.

Many patients in the series complained of symptoms which would indicate involvement of the nerve roots. In cases of injury in which the cervical segments of the cord were damaged it was difficult in some instances to ascertain whether there was sufficient evidence to warrant the diagnosis of the presence of a pathologic process involving the nerve roots. The radicular type of pain, various atrophies, contractures or sensory disturbances involving the upper extremity would lead one to

suspect trauma to the cervical nerve roots in many patients. Some of the patients presented no evidence of involvement of the cord, and yet there were neurologic syndromes present which, without doubt, could be explained only by the presence of a radicular lesion.

Patients with evidence of involvement of the nerve roots suffered neuralgic pains down the arms and weakness and atrophy of the various muscle groups of the scapula and humerus and of the arm, forearm and hand. Hypesthesias and paresthesias were also frequently present.

A syndrome referable to the head and neck, which was caused by either a bony or a ligamentous pathologic process, has been designated as a vertebral syndrome. The degree of the syndromes arising from involvement of the vertebral column, the nerve root and the spinal cord is given in table 2. In practically all of the cases there was a combination of one or more of these syndromes in the preoperative status of each case.

TABLE 2.—*Preoperative Status of Patients*

Case	Vertebral Syndrome	Nerve Root Syndrome	Cord Syndrome
1.....	None	Moderate	Severe
2.....	Moderate	None	None
3.....	Mild	Moderate	None
4.....	Mild	Mild	Moderate
5.....	Mild	Moderate	None
6.....	Moderate	None	None
7.....	Mild	Moderate	Mild
8.....	Moderate	Mild	None
9.....	Moderate	Mild	None
10.....	Moderate	Mild	None
11.....	Moderate	Mild	Severe
12.....	Moderate	None	Mild
13.....	Moderate	None	None
14.....	Mild	Moderate	None
15.....	Moderate	Mild	None
16.....	Mild	Moderate	None
17.....	Mild	Mild	Severe
18.....	Moderate	Moderate	Mild

PREOPERATIVE ROENTGENOGRAMS

Since there were only 10 cases in which preoperative and post-operative roentgenograms were available, only these will be referred to in connection with roentgenography. As a rule, anteroposterior and lateral views are taken of this type of lesion; however, stereoscopic and oblique roentgenograms are made in special instances. Special views are seldom necessary because these rarely give information in regard to the lesion which cannot be estimated from the routine views.

Anterior displacement was present in all of these cases, the amount of displacement of the luxated vertebrae varying from 5 to 80 per cent of the total horizontal diameter of the vertebral body. The amount of anterior vertebral tilt ranged from a minimum of 12 degrees to a maximum of 58 degrees, and tilt was present in all of the cases. Wedging constitutes a decrease in the vertical diameter of the involved

vertebra anteriorly, while compression constitutes a decrease in the vertical diameter both anteriorly and posteriorly. In many of the cases there was a combination of these. In 5 cases there was no wedging, while in the remaining 5 cases this varied from 6 to 17 per cent of the anterior vertical diameter of the involved vertebra. Compression was not present in 6 cases, and in 4 it ranged from a few to 20 per cent. A lateral wedging of 7 per cent was a feature in 1 case, while in the remaining cases this deformity was not present. Bony ankylosis was not found in any of the 10 cases studied roentgenographically. This is of interest in that the patients were seen many months and sometimes years after their primary injury had occurred.

In case 2 (fig. 1) the body of the fifth cervical vertebra was fractured vertically, with the anterior fragment displaced anteriorly 15 per cent and the posterior fragment displaced posteriorly 30 per cent. In case 9 (fig. 2) there was a fracture-dislocation of the fifth cervical vertebra, but the spinous processes of the fourth and the fifth cervical vertebra were widely separated. Separation should have taken place between the spines of the fifth and sixth cervical vertebrae, unless a fracture of the posterior elements was present. The roentgenographic appearance was indicative of a fracture of the posterior elements, and in this instance operative findings confirmed the diagnosis. Arthritic deposits were a feature in 1 instance and could well account for the complaints referable to the vertebral column. An ununited fracture of the arch could be seen in only 1 case, while in another instance there was the appearance previously noted which suggested a fracture.

In all of the cases in the series diagnosis as to the nature of the lesion was made by roentgenographic examination.

TREATMENT

In 3 cases in which the patient was seen fairly recently after injury an attempt was made to reduce the lesion. This was done by means of 10 pounds of traction on the head exerted with the head in a slightly extended position. Complete reposition of the involved vertebra was not accomplished in any instance, yet relief from pain was experienced by the patient, and the muscular spasm was diminished. Forceful extension was not used to reduce the lesion in any instance. Preoperative care consisted mainly in the partial immobilization of the spine by sand-bags placed on either side of the patient's head, while pain was relieved by rest and the use of sedatives. The patients were operated on within a few days after entering the hospital.

In 13 cases fusion of the spine was carried out. A combined one stage laminectomy and spinal fusion were performed in 5 other instances. When spinal fusion alone was done, the average operating time was one hour and twenty-five minutes; the longest operating time was one



Fig. 1 (case 2).—Roentgenogram showing severe compression fracture of the body of the fifth cervical vertebra.



Fig. 2 (case 9).—Roentgenogram showing a fracture-dislocation of the fifth cervical vertebra.

hour and fifty minutes, while the shortest time was forty-five minutes. In those cases in which the combined procedures were done the average operating time was one hour and fifty minutes. Two hours and thirty-five minutes was the maximum operating time, while the minimum was one hour and twenty minutes.

In 1 instance the operator attempted to replace the dislocated articular facets without success. In another instance a freely movable fractured arch was encountered. This was removed lest the cord be damaged at a later date. In 1 case further surgical work was done. In only 1 case were the coverings of the cord opened intentionally at the primary operation.



Fig. 3 (case 18).—Preoperative roentgenogram showing the greatest degree of anterior vertebral tilt and the greatest percentage of anterior displacement of the involved vertebra observed in any case in the series.

The Hibbs type of spinal fusion was carried out in all instances. This operation consists in the subperiosteal exposure of the laminae, spinous processes and lateral articulations of the vertebrae to be fused. The ligamentum flavum and cartilage from the lateral articulations were removed. Lateral articulations and their processes were then comminuted. Interdigitating bone chips taken from the spinous processes and laminae were turned in such a manner as to bridge across the intervening interlaminar spaces. In the 5 cases in which laminectomy was performed, a bilateral type of laminectomy was done, followed by fusion of the portions of the laminae which were not removed, as well as of the lateral articular processes.

During the operation the patient was in a prone position on the operating table, with the head supported in a head rest. The head rest consisted of a tripod with a horizontal padded loop, which fitted the conformity of the face. With this type of head rest the anesthetist was not hampered in his work, the patient was in a comfortable position, and his head could be changed at any angle desired by the operator.

Because of the proximity of vital centers, surgical intervention in this area of the spine is dangerous unless caution is practiced by the operator. The cervical segment of the spine lies rather deep, so that an extensive exposure is necessary. Usually exposure of the spinous processes of two vertebrae above and two below the seat of injury is required, as this will insure a sufficient operative field with the minimum of retraction force. When spinal fusion or laminectomy of this area of the spine is performed, it should be borne in mind that the posterior elements are smaller than elsewhere and the interlaminar spaces are wider. Needless to say, curetting of ligaments, turning down of bone chips or removal of the laminae should be done with the utmost care.

Immediately after the operation the usual care was the application of a few pounds of traction on the head with the head immobilized by sand-bags. In a few instances sand-bags alone were used, but traction on the head not only aids in immobilization but tends to relieve muscular spasm. The head is placed in a slightly extended position by means of a small pillow beneath the patient's shoulders. In this manner the proper position of the head is maintained until fusion becomes firm.

Constant nursing of the patient is imperative until he is fully conscious, lest the head be moved during the interval when he is recovering from the anesthetic. Even during the first few days postoperatively the patient can be turned from one side to the other at frequent intervals, traction on the head and the sand-bags, of course, being removed before turning. In this manner nursing care of the patient is facilitated, and the patient is made more comfortable. After two weeks the patient can be placed on his side for longer periods.

OPERATIVE FINDINGS

Among the more frequent findings which were noted at operation was the formation of scar tissue, and in a few instances old extravasated blood was found in the soft tissues about the spine posteriorly. Impingement of spinous processes and laminae was noted in 5 cases. In 7 cases ununited fractures of the posterior elements were found. In most of these the fractured portion of the vertebral arch was freely movable. Hypermobility luxated vertebrae were encountered in 6 cases. Complete bilateral dislocation of the articular facets was noted in 4

cases, while a severely crushed articular process was found in another case. Natural fusion of impinging laminae was present in 1 case. Frequently the laminae of the vertebra involved were displaced anteriorly, and in 3 instances these laminae were removed because they encroached on the cord. In 1 instance moderate anterior displacement of a lamina had caused an indentation on the cord.

POSTOPERATIVE COURSE

Little evidence of shock or other complications were present in these cases, and the immediate postoperative reactions were, as a rule, of a mild degree. An exception to this statement was a patient in whom



Fig. 4.—Postoperative roentgenogram showing solid bony fusion of the posterior elements while the involved vertebral body remains without bony ankylosis.

severe hemiplegia developed after spinal fusion, and further surgical treatment was later necessary. Slight edema of the occipital region and of the face was encountered postoperatively in 2 cases, and a generalized weakness of the extremities was present in 2. These complications lasted for only a few days, and no permanent damage was done to the cord. In a few cases there was a slight degree of abdominal distention, and in 2 cases urinary retention was present. These complications gave no alarm and were transient.

During their stay in the hospital all these patients, with the exception of those on whom further surgical measures were necessary, showed some degree of improvement in comparison with their preoperative status. The greatest and most constant improvement was in the amelio-

ration of symptoms arising from the vertebral pathologic process. Symptoms arising from involvement of the nerve roots were slightly improved but with little change in comparison to the preoperative condition. One patient with severe involvement of the spinal cord was greatly improved, while 2 with severe involvement were only slightly improved. Control of the sphincter muscle, however, had returned, and the patients were able to get about with the aid of crutches, whereas before they entered the hospital they had been bed-ridden.



Fig. 5.—Postoperative roentgenogram showing solid bony fusion of the posterior elements and bony ankylosis of the involved vertebrae.

With the exception of the 1 patient who came to secondary operation two weeks following the primary operation, the remaining 17 were allowed out of bed, with no supportive apparatus, in from six to twelve weeks postoperatively. These patients were discharged from the hospital wards in from seven to thirteen weeks postoperatively. The remaining patient in the series was discharged one year postoperatively. During the stay in the hospital this patient was in bed continuously.

FOLLOW-UP STUDY

The longest postoperative follow-up period in this group was six years and the shortest two months, while the average period was two years. After discharge from the wards the patients were seen at fairly frequent intervals in the dispensary. Almost immediately after discharge physical therapy in the form of massage of the cervical region, along with active and passive motion of the cervical portion of the spine, was started. Muscle training and reeducation of partially paralyzed groups of muscles were also carried out for a long period, while various mild contractures were dealt with by the aforementioned types of therapy as well as stretchings.

After spinal fusion of the cervical region in which two or more vertebrae are fused, one would naturally suppose that the mobility of the head would be limited to a considerable degree. However, this was not the case in this series, for 13 of the 18 patients presented free, unrestricted and painless motion of the head. In 5 instances there was a mild to moderate degree of limitation, mechanical rather than due to pain or spasm. One patient complained that he suffered from fatigue of the posterior cervical region. This would develop usually after he had been sitting for from three to four hours. In this case there was only 20 degrees extension of the head, and the patient held his head in a slightly flexed attitude. In this instance a portion of the cervical segment of the spine had been fused in a slight degree of flexion, causing an unnatural attitude of the head.

Fusion was reported as solid roentgenographically in 12 cases in from six to twelve weeks after operation. Postoperative roentgenograms were not made in 3 cases, while in 2 instances pseudarthrosis developed. Another patient required further surgical treatment a few weeks after the first operation had been performed. In those cases in which pseudarthrosis developed, repair was not attempted because neither of the patients had sufficient trouble to justify it.

By relieving these patients of preoperative vertebral symptoms of pain, crepitus and spasm, spinal fusion enabled them to move the head more freely than before operation. Also, the feeling of stability which is experienced after fusion of the spine dispels the fear which those patients had of moving the head.

Fourteen patients presented sufficient evidence preoperatively to be classified as having involvement of the nerve roots. Seven had moderate involvement and 7 mild. Two of those who had moderate involvement and 4 of those who had mild involvement preoperatively showed no evidence of irritation of the nerve roots at the follow-up examination, while 5 of those who had moderate involvement preoperatively showed involvement of a mild degree at the follow-up examination, and 3 of those who had mild involvement showed no change.

Ten cases in which preoperative and postoperative roentgenograms were available have been reviewed in connection with the relationship between anterior vertebral displacement and tilt in the presence of involvement of the nerve roots. Five of the patients had anterior displacement of the involved vertebra of from 20 to 8 per cent. Four of these had moderate irritation of the nerve roots preoperatively, while 1 presented no evidence of involvement. On their last visit to the dispensary 2 of the patients were without a nerve root syndrome, while 3 had a mild syndrome. Of 5 others with anterior vertebral displacement of from 0 to 20 per cent before and after operation, 1 had moderate and 4 had mild involvement of the nerve roots preoperatively, while postoperatively and on their last visit to the clinic, the patient with moderate involvement and 3 of those with mild involvement were relieved, while 1 patient still had a mild degree of irritation of the nerve roots.

Seven patients had anterior vertebral tilt of the involved vertebra of from 20 to 58 degrees both preoperatively and postoperatively. Four of these had moderate involvement of the nerve roots preoperatively, while 2 had mild involvement, and 1 had no evidence of injury to the nerve roots. After fusion, the moderate involvement in 2 patients decreased to a mild degree, and 2 of the patients presented no evidence of involvement. The 2 patients with mild involvement preoperatively had no evidence of injury to the nerve roots postoperatively, and the remaining patient was without any involvement, as before operation.

Three other patients had an anterior tilt of the involved vertebrae of from 0 to 20 degrees. One presented evidence of moderate involvement and 2 evidence of mild injury to the nerve roots. The patient who had moderate involvement preoperatively had mild involvement postoperatively; the condition of the patient with mild involvement remained the same, while the other patient did not show any evidence of involvement.

After operation and while these patients were in the hospital there was a definite improvement in the degree of irritation of the nerve roots in some cases. The improvement in the nerve root syndromes was gradual and steady, but after a few months little change was noted.

In comparing preoperative and postoperative roentgenograms, the percentage of anterior displacement and the degree of anterior vertebral tilt in these 10 cases did not change to a great extent. In some instances there was a decrease in the degree of tilt or displacement, while in others an actual increase had taken place. From the fact that so many of these patients were relieved of their nerve root syndrome by spinal fusion, and yet little or no correction of these deformities had taken place, one must naturally suppose that vertebral tilt of a moderate

degree, as well as vertebral displacement, if not accompanied by mobility, plays little part in the production of a nerve root syndrome in this type of lesion in its chronic stage.

Six of the patients in the series had a hypermobile luxated vertebra. Two of the patients had moderate involvement of the nerve roots preoperatively, while postoperatively 1 was without involvement, and the other had a mild degree. Two other patients with hypermobile luxated vertebrae had a mild degree of involvement preoperatively and none postoperatively. The remaining 2 patients had neither preoperative nor postoperative involvement. The number of hypermobile vertebrae in this series is small, and yet it may be misleading since the data in regard to gross pathologic changes at operation were very sketchy and incomplete. However, it is interesting to find that 4 of 6 patients with involvement of the nerve roots and with a hypermobile luxated vertebra were either completely or partially relieved of that involvement by spinal fusion. Perhaps the involvement of the nerve roots, which one so often finds as a feature in lesions of the cervical segment of the spine in the chronic stage, may well be explained by the presence of a hypermobile luxated vertebra. Certainly a very mobile vertebra, which is also luxated, can cause a strain on its nerve roots, while the elimination of motion of that vertebra by spinal fusion will produce a mitigation of a syndrome arising from involvement of the nerve roots. It might be assumed that patients in this series who presented such a syndrome but were not aided by spinal fusion did not have a hypermobile vertebra and that sufficient damage to the nerve roots or their coverings had been done at the time of the primary trauma to leave them in a chronically impaired state.

INVOLVEMENT OF THE CORD

Spinal fusion alone was done on 4 patients having involvement of the cord. One of these patients had mild preoperative and postoperative involvement, while another had mild preoperative involvement and severe postoperative involvement. The latter was the one with the severest displacement and tilt of the entire series, and there is no doubt that if, in the presence of such a degree of deformity, laminectomy had been done in conjunction with spinal fusion a far more desirable result would have been obtained. Moderate involvement was present in 1 patient preoperatively and mild involvement postoperatively, while another patient had mild involvement before operation and none after operation.

A one stage laminectomy and spinal fusion were carried out on 5 patients. Two of these had neither preoperative nor postoperative evidence of a syndrome, the laminectomy being done on 1 to remove

a very mobile fractured vertebral arch which at any time could have caused severe damage to the cord, while laminectomy was done on the other patient to remove a severely displaced vertebral arch. Laminectomy and spinal fusion were done on 3 other patients with severe involvement of the cord. In 1 of these there was a decided improvement in the cord syndrome, while 1 was relieved to a moderate degree, the remaining patient being slightly improved but still having severe involvement.

As has been mentioned before, the dura was incised at the primary operation in only 1 instance, and yet it was observed in many cases that the dura was thickened. I believe that in the presence of involvement of the cord, when laminectomy is done, the dura should be opened freely if it is at all thickened. An unyielding dura can cause as much

TABLE 3.—*Preoperative Status of Patients*

Case	Vertebral Syndrome	Nerve Root Syndrome	Cord Syndrome
1.....	None	Mild	Severe
2.....	None	None	None
3.....	None	Mild	None
4.....	None	None	Mild
5.....	None	None	None
6.....	None	None	None
7.....	None	Mild	Mild
8.....	None	None	None
9.....	None	Mild	None
10.....	None	Mild	None
11.....	None	None	None
12.....	None	None	None
13.....	None	None	None
14.....	None	None	Moderate
15.....	None	None	Severe
16.....	None	Mild	
17.....	None	Mild	
18.....	None	Mild	

pressure on the cord as a pressing vertebral arch, especially in the presence of anterior vertebral displacement or a kyphos.

Laminectomy in 1 case caused a decided improvement in the cord syndrome. By this procedure a severely displaced and fractured vertebral arch was removed. This had caused pressure on the coverings of the cord and on the cord. Neither the presence of a pressing arch nor a fracture of the arch was diagnosed preoperatively.

DISABILITY

The degree of disability of the patients in this series is based on the severity of the cord, nerve root and vertebral syndromes. Preoperatively 3 patients had a severe degree of disability, 13 a moderate degree and 2 a mild degree. Postoperatively, 2 of the patients had a severe degree of disability, 1 a moderate degree and 6 a mild degree, while 9 were without any form of disability. In other words, the results of treatment in 10 cases may be classified as excellent. Nine of the

10 patients having no cord, vertebral or nerve root syndromes had a normal degree of motion in the cervical portion of the spine. One of the patients presented severe involvement of the cord preoperatively, while postoperatively the involvement was of a mild degree. The results in 5 cases were classified as good, i. e., a marked decrease in the severity of the syndromes had taken place. The results in 1 case were fair, while in 2 they were poor. In 1 of the latter cases the patient was much worse than before operation, while in the other case the patient was improved slightly but was still severely handicapped.

In table 3 is given the postoperative status of each patient.

CONCLUSIONS

1. Closed reduction of a fracture-dislocation or dislocation of the cervical portion of the spine in many instances fails to restore the patient to normal.

2. The disability of the patient should be estimated in regard to the degree of involvement of the vertebral column, the nerve roots or the cord.

3. The type of involvement of the cord is difficult to ascertain in a case of a lesion of this nature.

4. An ununited fracture of the vertebral arch is common in such cases and is difficult to diagnose.

5. Natural fusion of the vertebral bodies of the involved vertebra does not occur in a number of cases.

6. Hypermobility of the luxated vertebra is the cause of involvement of the nerve roots in many cases.

7. Spinal fusion of the cervical region is not a dangerous procedure in experienced hands.

8. Spinal fusion is of little value in the treatment of syndromes arising from involvement of the cord, but if possible a combined laminectomy and spinal fusion should be attempted in the presence of involvement of the cord and anterior vertebral displacement.

9. If laminectomy is done, the coverings of the cord should be freely opened if they are at all thickened.

10. Spinal fusion relieves a patient of symptoms referable to the vertebral pathologic processes and is the only adequate means to stabilize a hypermobile luxated vertebra.

11. The mobility of the head and neck is not materially limited by fusion of three or four cervical vertebrae.

12. Anterior vertebral tilt and displacement without mobility play little part in the production of nerve root syndromes.

CLEFT PALATE

A CORRELATION OF ANATOMIC AND FUNCTIONAL RESULTS FOLLOWING OPERATION

WALLACE P. RITCHIE, M.D.

ST. PAUL

The operation for cleft palate was presented for the first time comprehensively, according to Dorrance, in 1816 by von Graefe, the founder of modern plastic surgery. The operation which is known today as the Langenbeck procedure was described in 1861 by von Langenbeck.

An extensive literature has accumulated since these early operations for cleft palate, and but a small amount of it pertains to the functional results after treatment.

Reports on the phonetic outcome in a group of cases may be satisfactory individually, but great difficulty is encountered in comparing the results in one group with those in another. The difficulties of judging the phonetic results of other investigators arise because, in the first place, the observations made for each report depend on the auditory sense, which is individually variable. Second, there are so many factors involved in speech that a method of analysis satisfactory to one observer might not meet the demands of others. Third, the problem of a foreign tongue makes the task of comparison more difficult, for it is probable that certain languages may be more perfectly spoken by a person with a cleft palate.

Ideally, the most accurate evaluation of phonetic results can be obtained only by a trained phoneticist. However, this ideal is difficult to obtain.

The main purpose of this work is to correlate the speech defect with the anatomic result and to make the observations in as simple a manner as possible and by a method which can be carried out by one with no special training in phonetics.

REVIEW OF THE LITERATURE

Whitehead first tabulated the phonetic results in such cases in 1870. Of five patients who had undergone repair for a cleft palate, one had

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distinct speech, two showed improvement in speech, one had "intelligent speech" but with some nasalization and one wore an obturator.

Bond stated in 1893 that he had never seen a person with a corrected cleft who did not have some speech difficulty.

Kappeler in 1902 stated that it is rare to obtain normal speech without training. Of sixteen patients who did not receive training and did not use an obturator, four had normal speech, one showed noticeable improvement and eleven showed no improvement. Of thirteen who received speech training only, eleven had normal speech, and two showed noticeable improvement. Of twenty-nine who received speech training and also used an obturator, twenty-three had normal speech, and six showed noticeable improvement.

Church in 1904 disagreed with the widely accepted opinion that distinct speech could be acquired by a person with an unrepaired cleft palate.

In 1904 Ranzi and Sultan reported the results in one hundred and one cases. In six, speech was normal; in forty-four, there was improvement; in fourteen, the functional result was not successful; in twelve the operation was unfinished, and in twenty-five, the results were not known.

Berry reported the results in two series of cases. Of the first series of sixty-one cases, reviewed in 1905, he stated: "In no case has speech after operation become absolutely normal, and there are comparatively few in which I should call it very good." According to his data, speech was very good in five cases, good in eighteen, fair in fourteen, indifferent but improving in three, bad in four, already much improved in eight and not yet improved in four. Three of the patients had not yet learned to speak, and no report had been received concerning eight.

In the second group of eighty-one cases, reviewed in 1911, he stated that there were some cases in which speech was so nearly perfect that it was difficult to detect anything wrong. The results are tabulated separately for individual cases. An analysis shows that the results are apparently more favorable than those in the previous series.

Brown in 1908 stated that the ultimate result is measurable only by the perseverance by which continued speech training is received. He noticed that the parents of many children with cleft palate had some speech defect which may have been either a nervous inefficiency in speech mechanism or a slight imperfection of anatomic development, either of which became a cleft in the next generation. He also stated that scars of the lips disturbed the articulation of b, f, m, p, v and w and that in many cases the articulation of c, d, g, h, j, k, l, n, r, s, t and z was poor because all of these sounds, which are uttered by the tongue behind the teeth, were distorted by an imperfect arch and teeth caused by ill advised operations in infancy.

Blakeway stated, in comparing results of different operations in 1914, that of seventeen persons operated on by the Lane technic there were five who were old enough to speak, and all of these were poor speakers.

Brophy stated in 1914 that "if operation is properly performed early, no defect is noted in phonation." He also stated that if operation is performed between the ages of 2 and 12 more or less defect in speech will remain unless the patient is properly trained by one who understands speech.

Stahl in 1923 reported the following results in thirty-one cases: In ten speech was perfect; in eight, good; in seven, fair; in two poor, and in four, very poor.

Monnier reported the results in ninety-three cases in 1924. In twenty-two speech was good; in thirty-four, good with slight nasalization; in fifteen, distinct with marked nasalization, and in twelve, indistinct, while in ten the patient had not yet learned to speak.

Barrington-Ward in 1927 reported that speech was good in twenty of fifty-seven cases, fair in eighteen and bad in twenty. Four of the persons with bad speech were mentally defective.

Tschmarke reported normal speech in 9.1 per cent of forty-five cases, improved speech in 57.6 per cent and unimproved speech in 33.3 per cent. He presented the following tabulation in which are compared the percentage of well healed palates and the satisfactory functional results obtained by different authors:

Author	Healed Palates	Satisfactory Functional Results
	%	%
Kappeler	86.5	53.3
Ranzi and Sultan	69.3	9.3
Stahl	58.7	15.0
Veau and Ruppe	74.0	25.0
Dreher	60.9	34.7
Tschmarke	64.3	9.1

Turner stated that of forty-four cases in which the palate was completely restored, speech was normal in seven, good in twenty, fair in fourteen and bad in three.

Halle stated that in most instances if operation is performed in the first year speech will be normal or almost normal.

Nitch in 1927 obtained good speech in thirteen of thirty-five cases, poor speech in seventeen and bad speech in five.

Burdick in 1930 remarked that no matter how successful an operation is and no matter what type of operation is performed the speech will be far from normal. He obtained good results in nine of twenty-three cases of incomplete cleft and in six of twenty-two cases of complete cleft.

Pagnamenta in 1932 tabulated his anatomic and functional results. These are presented in table 1.

In 1929 Veau reported the phonetic results in one hundred cases in which the classic procedures of Langenbeck or one of its modifications was used. The speech of ten of the patients improved rapidly, and they spoke well or nearly normally; the speech of six was improved by phonetic education and presented little, if any, defect. Twenty-four of the patients had poor speech with little intelligibility.

In 1922 Veau reported the ultimate functional results of forty in which his procedure was used. Thirty-five per cent of the patients had normal phonation; 29 per cent had good speech but with nasal air and bad nasalization, and 36 per cent had vocal deficiency in that they were unable to produce certain sounds such as p, t and k or ch, s, j and z.

In 1933, in a second series of one hundred cases, he found 62 per cent of the patients with normal speech, 23 per cent with the nasal air and nasalization and 15 per cent with vocal deficiency.

TABLE 1.—*Anatomic and Functional Results of Pagnamenta*

Type of Cleft	Number of Cases	Good Palates, %	Under- standable Speech, %	No Nasali- zation, %	Slight Nasali- zation, %	Severe Nasali- zation, %
Partial cleft	27	55	77	29	14	5
Subtotal cleft	45	39	63	21	46	33
Total unilateral cleft with lip defect.....	54	30	55	15	43	42
Total bilateral cleft with lip defect.....	16	23	42	0	35	65

Throughout all his work Veau stressed the fact that a good anatomic result is essential for a good functional result regardless of speech training. Of one group of forty patients with normal speech, twenty-four had had no speech training. Of the sixteen who had to be reeducated, fifteen spoke before operation.

Other articles, by Veau and Borel, and Ruppe and Ruppe, give their methods for analyzing and training of speech.

MECHANISM OF CLEFT PALATE SPEECH

There are two main characteristics of speech which are noted in practically all cases of cleft palate: (1) disturbed quality of tone and (2) disturbances of articulation.

1. A disturbed quality of tone is exemplified by what is commonly known as "nasalization," "nasaling," "nasal tone" or "talking through the nose." The term nasalization will be used in this analysis. It is also exemplified by a lack of what is usually termed "resonance" and also of "inflection," thereby giving the flat, uninteresting monotone so characteristic of the person with a cleft palate.

The following is an interpretation of this disturbed quality of tone after a study of the current texts on speech and voice:

After a column of air which has been put into motion by the lungs, intercostal muscles, diaphragm and abdominal musculature passes through the larynx, it emerges with a sound which has two characteristics, pitch and intensity.

The pitch is determined by the number of vibrations of the vocal cords and is the result of a fundamental tone plus a range of overtones or undertones, called partials. Ordinarily the ear is not aware of these partials, as they, together with the fundamental tone, are heard as one sound with a definite pitch.

When the column of air, which now has pitch and intensity, reaches the pharyngeal, oral and nasal cavities, it enters into "resonating" cavities. These cavities have the power to set up vibrations which differ according to their size and shape. The number of vibrations may equal the vibrations of the fundamental tone, in which case this tone is augmented; or the number of vibrations may equal those of one of the partials, in which case that particular partial is augmented, or a number of different vibrations may be set up at the same time augmenting a combination of partials. The result of this modification of the original tone by the vibrations set up in the upper respiratory passage adds a third characteristic to the original tone, a quality or timbre.

This addition of quality is well demonstrated by Bell:

Press your lips firmly together while you blow air between them, so as to cause the edges to vibrate. The sound produced is not very pleasant and resembles, more than anything else, the hum of a bee But place the buzzing lips at the end of a tube, for example, a trumpet, and at once the quality changes In this case the source of the sound is found in the vibration of the lips but the timbre or quality is due to the trumpet.

Any change in the resonating cavities of the upper respiratory passages will change the quality of a sound.

There are three main defects in these cavities in cases of cleft palate which tend to change the quality of a sound.

(a) The first is defective closure of the velopharyngeal sphincter. This defect permits the column of air to be shunted away from the normal resonating chamber, the mouth, to an abnormal one, the nose. It not only gives the flat monotone speech characteristic of a person with a cleft palate but also is the cause of nasalization. This deformity is by far the most serious of the three defects and the resulting quality of sound is called *rhinolalia aperta*.

(b) Changes in the size and shape of the chambers, giving an abnormal nasal resonance, is the second cause of defective quality of speech. Nasal resonance of some degree is a part of all normal speech and is acquired by vibrations set up in the nasal cavities by the column of air below the closed velopharyngeal sphincter trans-

mitting its impulses through the soft palate, thus adding a nasal quality to the resultant tone. That the patient with a cleft palate usually has a nasal passage of abnormal size and shape is commonly recognized. This abnormality is most frequently a narrowing of the nasal cavities, by a deformed septum, enlarged turbinates or enlarged adenoids. The resulting defect in quality of sound is called *rhinolalia clausa* and is exemplified in a person who has a cold.

Cleft palate speech, which is usually characterized by both of the aforementioned defects in quality, *rhinolalia clausa* and *rhinolalia aperta*, is designated as *rhinolalia mixta*.

(c) The third anatomic defect which may disturb the quality of a tone is less important but must play some rôle, although it is impossible to analyze it separately. This defect consists of the scar tissue and taut mucous membrane surfaces which result from the operation and which undoubtedly hinder the vibrating property of these surfaces.

2. Disturbances of articulation, the second characteristic of speech noted in the majority of cases of cleft palate, has been well summarized by Hudson Makuen. According to him, normally consonants are made

... by impeding the column of air of breath at certain points above the larynx. The points at which this impediment takes place are called the stop positions. These have been divided into the anterior, middle and the posterior stop positions. The anterior one is formed by the lips (in the articulation of the so-called labial sounds, p, b, m, wh, w), by the lower lip and teeth (in the articulation of the labiodentals f and v) and by the tip of the tongue and teeth (in the articulation of the linguo-dentals th and ch); the middle one by the tongue and the hard palate (in the articulation of the anterior-linguo palatals s, z, sh, t, d, n, l); and the posterior one, by the dorsum of the tongue and soft palate (in the articulation of the posterior linguopalatals r, g, h, y). For all these sounds requiring an impediment in the outgoing column of breath, whichever stop position may be used, it is necessary to have a freely movable and normal palate.

In the cleft palate which has not been repaired, the anterior and middle stop positions are rarely used because of the inability of the patient to focus his vocalized breath at this point when there is a free passage for air through the nasal cavity. The patient uses substitute stop positions, such as the anterior nares, the base of the tongue and the posterior pharyngeal wall and the lips of the larynx formed by the arytenoid cartilages and the arytenoid and aryepiglottic folds.

When perfect closure of the velopharyngeal sphincter is obtained after operation, this habit of using substitute stop positions is one of the major causes of poor speech.

ANATOMIC CONSIDERATION

Dorrance, Whillis and Wardill have presented this subject with special emphasis on the sphincteric action of the muscles of the soft palate and the posterior pharyngeal wall.

The "velopharyngeal sphincter" is a well established entity, and hereafter insufficient approximation of the soft palate with the posterior pharyngeal wall will be described as velopharyngeal insufficiency.

MATERIAL AND METHOD OF USE

This report concerns one hundred cases of cleft palate in which an operation was done for repair.

The records of seventy-five cases were obtained from the files of Dr. H. P. Ritchie. Those of thirteen cases were obtained from the files of the Special Class Department of the Minneapolis Board of Education and concern children who had had speech training in the city schools at one time or another. The data on the remaining twelve cases were obtained at the University of Minnesota Hospital Dispensary as the patient returned for a routine check on his condition. All patients observed were used for this study except a few who were too young to cooperate or those who refused to talk.

The greater portion of the patients were operated on by Dr. H. P. Ritchie or by one of his associates. The type of operation has not been recorded in the study of each case. However, the majority of persons were operated on by the fundamental Langenbeck procedure with suturing of raised mucoperiosteal flaps in the midline, muscle suture of the soft palate with a figure of eight suture and occasional wiring of the premaxilla, as described by Ritchie. In the last few years the wiring of the alveolar process has been discontinued, except in cases in which the defect is of unusual degree, and instead the lip is repaired as a preliminary procedure to mold the alveolar process by muscle pull.

The sounds and words used in the phonetic outline have been suggested by Dr. Bryngelson, of the University of Minnesota Speech Clinic, and are taken from his outline on articulatory speech disturbance, which is a modification of the Travis-Rasmus speech sound discrimination tests.

All of the cases were grouped in the manner suggested by Davis and Ritchie in 1922, which is briefly:

Group I. Lip cleft.

Group II. Palate cleft (normal lip and alveolar process), designated according to the length of the cleft of the hard palate as $\frac{1}{4}$, $\frac{2}{3}$ or $\frac{3}{4}$ and cleft of the soft palate only.

Group III. Lip, alveolar process and palate cleft, designated as right, left or bilateral and complete or incomplete, i. e.:
 Right complete or right incomplete
 Left complete or left incomplete
 Bilateral complete or bilateral incomplete

TABLE 2.—Outline Used For Analysis of Phonetic Results After Operation
in Cases of Cleft Palate

Father's name.....	Address.....	
Patient's name.....	Birth date..... Age.....	
Patient's group.....	Hospital and record number.....	
Phonetic education.....		

I. Lip:

Form.....	Operation date.....		Interval.....
Examination: 1. Nostrils: Contour.....			
2. Body of lip: Looks..... Motion.....			
3. Speech:			
Letter	Initial	Medial	Final
	Result		
O	{ old		
	{ so		
	{ The old oak stood so much alone		
U	{ unit		
	{ use		
	{ Few argue and use cues as fuel		
B	{ base	may be	cab
	{ Baby Bee bit her boots		
P	{ pay	paper	ape
	{ Paul slipped on a potato peel		
M	{ May	camel	same
	{ May made mama maim the man		
V	{ vain	ivy	save
	{ Veal was divided in five parts		

Comment:

II. Process:

Form.....	Operation date.....		Interval.....
Examination: 1. High..... Median..... Low.....			
2. Speech:			
Letter	Initial	Medial	Final
	Result		
T	{ tail	city	sit
	{ Tom ate ten tomatoes		
D	{ do	daddy	fade
	{ Fido is Freda's poodle		
Ch	{ chart	catcher	patch
	{ The pitcher changed his church		
Th	{ then	others	path
	{ Then the path of others was strengthened.		

Comment:

III. Palate—Hard:

Form.....	Operation date.....		Interval.....
Examination: 1. High..... Median..... Low.....			
2. Speech:			
Letter	Initial	Medial	Final
	Result		
Y	{ year	yo-yo	
	{ Yale men yelped at the Yeoman		

Comment:

IV. Palate—Soft:

Form.....	Operation date.....		Interval.....
Examination: 1. Anatomy:			
a. Uvula.....			
b. Motility: 1..... 2..... 3..... 4.....			
c. Texture: Full..... Soft.....			
Thin..... Hard.....			
d. Approximate length..... Long.....			
Median.....			
Near.....			
e. Approx. dist. to post. pharyngeal wall..... Long.....			
Median.....			
Near.....			
f. State when "Ah"			
Approx. dist. to post. pharyngeal wall..... Long.....			
Median.....			
Near.....			
Superior constrictor muscle.....			
Well developed.....			
Underdeveloped.....			
Insertion of levator.....			
Prominent.....			
Not prominent.....			

TABLE 2.—Outline Used For Analysis of Phonetic Results After Operation in Cases of Cleft Palate—Continued

2. Functional:				
a. Functional test.....				
b. Speech:				
Letter	Initial	Medial	Final	Result
K	{ cape	ache	racket
	{ Keep cool if you can		
G	{ get	agony	lag
	{ The rogue stole the goose		
Ng		slinging	hang
Comment:				
General Impression: Anatomic Result:				
	Lip.....			
	Process.....			
	Palate (hard).....			
	Palate (soft).....			
	Functional Result.....			

Table 2 presents the type of outline used in each case.

It has been the purpose in this study to follow the suggestion of the classification of Davis and Ritchie and take up each cleft separately, viz., the lip, the alveolar process, the hard palate and the soft palate, and to choose sounds which are made for the most part by these structures and from which any deviation from the normal can easily be ascertained.

For the lip itself, b, p, and m are used. O, u and v were also used, although not true labials, because the lip is used in a different manner than b, p and m.

For the alveolar process, sounds classified not only as linguodentals, such as ch and th, but as anterior linguopalatals, such as d, t and s, were used. The latter are used in the test for the alveolar process instead of for the hard palate because they are articulated at the junction of the alveolar process and the hard palate.

For the hard palate, y (j) was the sound used. Reference was also made to the anterior linguopalatals of the preceding group.

For the soft palate, k and hard g as well as ng were used. In this analysis the anatomic study was more comprehensive. The motility was graded in degrees from 0 to 4, the latter being that of a normal palate.

No accurate measurements by linear scales were made. Estimations of the length of the repaired palates were recorded. After fifty of these had been recorded, the average length was estimated. Those palates of average length were recorded as normal; those longer than average were recorded as long, and those shorter than average were recorded as short.

The same procedure was carried out for the estimations of the distance from the palate to the posterior pharyngeal wall in the quiescent state and also when "Ah" was said.

Comparisons were not with the normal palate. Similar estimations on twenty-five normal palates indicated that the average length of the normal palate was longer than that of the cleft palate, and the average distance to the posterior pharyngeal wall both in the active and in the quiescent state was shorter in the normal than in a cleft palate. Consequently, when a cleft palate was designated as long, it was long as compared to the average length of a group of cleft palates and not to the length of a normal palate.

The consistency of the soft palate as well as the development of the superior constrictor muscle and the prominence of the insertion of the levator muscles were also recorded.

The functional test used in the majority of cases was performed as follows: A small piece of rolled paper was placed on the surface of each of two pieces of cardboard, measuring about 3 by 2 inches. One of these was held just above the vermilion border of the upper lip and the other just below the vermilion border of the lower lip. The patient was then told to blow the piece of paper off the lower one. If any air escaped through the nose, the piece of paper on the upper cardboard also moved or was blown off the card, showing that there was incompetent closure of the velopharyngeal valve.

ANALYSIS OF MATERIAL

The purpose of this analysis, as previously stated, is to determine to what degree and manner the anatomic defect influences the functional result after operation.

One hundred cases were studied. Seventy-seven were classified as belonging to group III. In fifteen of these the cleft was bilateral, and in sixty-two, either right or left unilateral. In two of the fifteen cases of bilateral cleft the palate was normal. Twenty-three cases were classified belonging to group II. Twenty of these were placed either in group II 1/3, group II 2/3 or group II 3/3. Only three were classified as belonging to group II, cleft of the soft palate only.

The sounds used for the analysis were the consonants, except in one instance, in which o and u were used. The phonetic defect of these consonants is usually made up of two elements. The first is a result of insufficient closure of the velopharyngeal sphincter, resulting in nasalization. The second is the articulatory defect, which may be the result of nasalization but to which is added the defect caused by an anatomic fault at a stop position.

In every case an attempt was made to establish the relative importance of insufficient closure of the velopharyngeal sphincter and the anatomic stop position.

Correlation as Regards Defects of the Lips.—The lip is the labial portion of the anterior stop position. B, p, m, v, o and u were the sounds used. This part of the study included only the cases in group III, in which the clefts were bilateral or unilateral and complete or incomplete. In none of the cases in group II was there an anatomic defect of the lips.

Whether the phonetic defect was in the initial, medial or final stop position is designated by numerals 1, 2 and 3. A defect of an initial p is designated as p 1, of a medial p as p 2 and of a final p as p 3. The same procedure is used throughout for all the stop positions, whether the lips, the alveolar process or the palate are being studied.

An analysis of the phonetic results in those cases in which there was a defect of the lip is given in table 3. A discussion of this table follows:

B 1 was absent in one case (67) and faint in another (21), while p 1, 2 and 3 was omitted in one case (37). There was some degree of nasalization in all these cases, and as the main cause for omission of sounds is inability to focus the air on the correct stop position, due to imperfect closure of the velopharyngeal sphincter, this nasalization rather than the anatomic defect of the lip can be held responsible for the phonetic defect.

B 1 and p 1 were articulated through the nose in one case (33). There was no anatomic defect of the lip in this case, but nasalization of 2 degrees was the cause of the phonetic defect.

U 1 was slightly indistinct in one case (15). The function of the lips was good in this case, but there was nasalization of 4 degrees, which in all probability caused this defect.

The most common defect was the substitution of b for p, m for p or m for b. In all of these cases except case 29, there was some degree of nasalization. With nasalization present, the tendency is to use the sound which is made by a similar architecture of the stop position but which requires less perfect closure of the velopharyngeal sphincter.

In one case (29) there was no anatomic defect of the lip and no nasalization, yet the patient substituted m for b 1. The record of this case showed that the patient talked perfectly if the speech was slow and that the phonetic defect occurred only when the speech was rapid. This demonstrates the occasional case in which there is perfect anatomic function but the patient has not developed the power to move the soft palate rapidly.

In view of the results of this analysis, the conclusion is that as far as the labial element of consonants is concerned the patients in group III can adequately compensate for any anatomic defect of the repaired lip.

Correlation as Regards Defects of the Teeth, Alveolar Process and Extreme Anterior Part of the Hard Palate.—The linguodentals, such as th, ch and s, and the anteriopalinguopalatals, t and d, were employed in this analysis. There were four types of functional defects and fourteen variations of anatomic defects. The number of functional defects outnumbered the anatomic defects, as there were two separate types of functional defects in twelve cases. Thus the totals have no reference to the number of cases (table 4).

1. Slur of ch or s or both. The recording of this defect was the most difficult of all, for if one critically analyzes a group of normal

TABLE 3.—*Analysis of Functional Defects in Relation to Anatomic Defects of the Lips*

Case	Anatomic Defect	Functional Defect	Nasalization, Degree
9.....	Short lip	None	0
13.....	Short lip	None	0
23.....	Short lip	None	0
34.....	Short lip	p 1 = b 1	3
57.....	Short lip	None	2
15.....	Abnormal scar	u 1, slightly indistinct	4
22.....	Abnormal scar	None	2
24.....	Abnormal scar	b 1 = m 1	1
40.....	Abnormal scar	None	2
55.....	Abnormal scar	None	—1
63.....	Abnormal scar	None	1
20.....	Muscle out of contact	None	2
62.....	Muscle out of contact, large hole in hard palate also	b 1 = m	1
26.....	Tight lip	None	1
50.....	Tight lip	None	1
37.....	Notch in vermillion border	p 1, 2, 3 omitted	1
46.....	Notch in vermillion border	None	0
53.....	Notch in vermillion border	None	0
41.....	Poor motion	None	0
67.....	Poor motion	b 1 = m, b 1 omitted	3
8.....	No anatomic defect	p 1 = b 1	1
21.....	No anatomic defect	b 1, faint	1
29.....	No anatomic defect	b 1 = m	0
33.....	No anatomic defect	v 1 = b; b 1 and p 1, through the nose	2
60.....	No anatomic defect	b 1 = m	3
61.....	No anatomic defect	b 1 = m	2
93.....	No anatomic defect	b 1 = m	1

persons. the probabilities are that a slight slurring element will be found in many of them on the articulation of the sibilants.

In forty-two of the sixty-five cases, or 64 per cent. there was some degree of slurring of ch or s. In some cases it was extremely difficult to determine whether there was a sufficient degree of slurring to class it as a defect, but if there was the slightest question it was recorded as such.

This defect, although the most frequent, is by far the least important as far as the general speech of the patient is concerned. In fourteen of the forty-two cases, or 25 per cent, in which the results in regard to speech were ultimately classed as excellent, this defect of slurring of ch or s was so slight that there was no hesitation in classifying the results as excellent.

The question as to whether the anatomic defect of the stop position has more influence on this functional defect than the degree of velopharyngeal insufficiency is difficult to determine.

The fact that in thirty of the forty-two cases, or 71 per cent, some degree of velopharyngeal insufficiency was present would lead one to conclude that the latter element is an extremely important one.

On the other hand, it was noted that the degree of nasalization was minimal in practically all of these cases. As only a moderate force is needed to articulate a good *ch* or *s*, it is quite possible that perfect closure is not absolutely necessary for a good *ch* or *s* and that a minimal degree of nasalization plays no rôle in slurring of *ch* or *s*.

TABLE 4.—Incidence of Functional and Anatomic Defects

Functional Defects	Incidence
1. Slur of <i>ch</i> , <i>s</i> , or both.....	42
2. <i>Ch</i> or <i>s</i> or both spoken through the nose.....	10
3. Omission of <i>s</i> , <i>ch</i> 1, 2, 3; <i>d</i> 1, 2, 3 or <i>t</i> 1, 2, 3.....	16
4. Substitution: <i>d</i> = <i>n</i> , <i>t</i> = <i>d</i> = <i>n</i> , <i>s</i> = <i>n</i>	5
5. Absence of functional defect; anatomic defect.....	5
Total.....	77
Anatomic Defects	
1. Atrophied premaxilla.....	2
2. Malocclusion.....	4
3. Notch in alveolar process.....	4
4. Orthodontia.....	8
5. Teeth out of line.....	16
6. Tooth misplaced posteriorly.....	5
7. Tooth misplaced anteriorly.....	1
8. Teeth abnormally spaced.....	4
9. Small hole anterior to alveolar process.....	8
10. Overlapping of medial with lateral process.....	4
11. Overlapping of medial by both lateral processes.....	1
12. Teeth in poor.....	1
13. Short process,.....	2
14. No teeth present.....	1
15. Absence of anatomic defect; functional defect.....	4
Total.....	65

Furthermore, the contour of the teeth plays an important rôle in the articulation of the sibilants, and as the greatest number of cases of defective articulation were observed in persons in whom the contour of the teeth was defective, the probabilities are that a defective contour and not defective closure of the velopharyngeal sphincter was responsible for a slur of *ch* or *s*.

The fact that one observes this functional defect in many normal children who have an extremely irregular contour of teeth strengthens this impression.

Thus one concludes that the anatomic defect of the teeth and the alveolar process is responsible for slurring of *ch* or *s* and that defective closure of the velopharyngeal sphincter plays no rôle.

2. *Ch* or *s* or both spoken through the nose. There were ten cases in which this defect was present, and in nine some degree of

nasalization was present. In the one case in which no velopharyngeal insufficiency was present there was a small hole anterior to the alveolar process which may have been the cause of the defective articulation.

In two of the cases there were holes in the anterior part of the hard palate. Holes in the anterior part of the hard palate tend to cause an omission of sounds rather than articulation through the nose, as will be demonstrated in the analysis of persons with defects of the hard palate. Therefore, in these two cases the defect was more than likely due to velopharyngeal insufficiency rather than to the holes in the hard palate.

The anatomic defects in this group of cases were as follows: an atrophied premaxilla, one case; malocclusion, one case; orthodontia, two cases; teeth out of line, two cases, and a tooth misplaced posteriorly, one case. In one case there was no anatomic defect of the process but a marked degree of velopharyngeal insufficiency.

As no type of defect of the alveolar process was consistently found in the persons who articulated *s* or *ch* through the nose and as velopharyngeal insufficiency was consistently found, the probabilities are that the poor function of the velopharyngeal sphincter was responsible for the phonetic imperfection of articulating *ch* or *s* through the nose rather than any anatomic defect of the alveolar process.

3. Omission of *s*, *d*, *ch* or *t*. There were fifteen cases in which this defect was present. The anatomic defects were as follows: malocclusion, two cases; teeth out of line, four cases; a tooth misplaced posteriorly, one case; teeth abnormally spaced, one case; a small hole anterior to the alveolar process, two cases; overlapping of the medial with the lateral process, one case, and overlapping of the premaxilla by a tooth, one case.

In fourteen cases, or 93 per cent, there was some degree of velopharyngeal insufficiency. In six cases there were holes in the hard palate, besides, the majority being in the anterior part of the hard palate or extending into it.

In one case in which there was no nasalization, the patient had no difficulty with the labial or soft palate consonants, and therefore the probabilities are that the phonetic defect present was due to incorrect habits acquired before operation. The fact that the operation had been performed only six months before this analysis strengthens this impression.

No consistent anatomic defect was found in the alveolar process, whereas velopharyngeal insufficiency was common to all except the one mentioned. This would tend to show that the defect in the alveolar process was not responsible for this phonetic defect but that the inability to close the palate sphincter was the cause.

The question whether or not the omission of these consonants in the six cases in which there were holes in the hard palate was due to these holes or velopharyngeal insufficiency is difficult to determine. Holes in the anterior portion of the hard palate often cause omission of these consonants. These holes were present in only six cases, whereas velopharyngeal insufficiency was present in fourteen. Thus, there were eight cases in which the only anatomic defect was incompetency of the velopharyngeal sphincter.

The impression is that in the omission of the anterior linguopalatal sounds velopharyngeal insufficiency is responsible rather than a defect in the alveolar process unless a hole is present in the hard palate, in which case both anatomic defects are probably responsible. The velopharyngeal defect is possibly the more important of the two.

4. Substitution— $d=n$, $t=d=n$, $s=n$. There were five cases in which this phonetic defect was observed. In all there was some degree of velopharyngeal insufficiency.

As was the case in the articulation of the labial consonants, the consonants requiring less perfect closure of the velopharyngeal sphincter were substituted.

In general, therefore, in persons with defects of the alveolar process velopharyngeal insufficiency plays the major rôle in articulation of the consonants, except the sibilants, in which case the anatomic defect of the alveolar process is more important.

Correlation as Regards Defects of the Hard Palate.—There were twenty-one cases in this group. In fourteen there was no functional defect. In the seven cases in which there were both functional and anatomic defects, four of the patients omitted one or more of the consonants, two spoke the consonants indistinctly and one substituted. All had some degree of nasalization.

Of the twelve cases in which small holes from 1 to 2 mm. in diameter were found in the hard palate phonetic defects were noted in only two. In one case (34) the patient substituted t for d . Velopharyngeal insufficiency of 3 degrees undoubtedly was the cause of this defect. In the other case (74), the patient pronounced y indistinctly. Nasalization of 1 degree may have been the cause for this.

In one case (62) a large hole was present in the anterior part of the hard palate, yet in some way the patient articulated all the consonants extremely well. The impression was that the tongue was used to plug the defect.

In one case (91) there were two large holes, one on each side of the palate where lateral incisions had been made. Each hole was 1 by 1 cm. in diameter. The phonetic defect present was a mixture of the more common nasalization plus a quality which is noticed in one who

attempts to talk with hot food in the mouth. This "hot food" quality was also noted in case 63.

In one case (61) a hole measuring 1 by 1 cm. was present at the junction of the hard and the soft palate. All the initial consonants, including k and g, were omitted. Nasalization of 2 degrees was also present, which may have accounted for the omission of the anterior and middle stop position consonants but possibly not for the posterior stop position sounds, k and g.

In two of the four cases in which the patient omitted the consonants there were holes in the anterior part of the palate and in two there were holes in the posterior part of the hard palate.

TABLE 5.—*Analysis of Functional Results in Relation to Anatomic Defects of the Hard Palate*

Case	Anatomic Defect	Functional Defect	Nasalization, Degree
2	Hole, midpalate, 1-2 mm.	0	0
5	Hole, midpalate, 1-2 mm.	0	0
12	Hole, midpalate, 1-2 mm.	0	0
19	Hole, midpalate, 1-2 mm.	0	0
21	Hole, midpalate, 1-2 mm.	0	1
30	Hole, midpalate, 1-2 mm.	0	2
34	Hole, midpalate, 1-2 mm.	t 1 = d 1	2
46	Hole, midpalate, 1-2 mm.	0	0
49	Hole, midpalate, 1-2 mm.	0	0
53	Hole, midpalate, 1-2 mm.	0	0
74	Hole, midpalate, 1-2 mm.	Indistinctly	1
43	Hole, midpalate, 1-2 mm.	0	0
61	Hole, 1 by 1 cm., junction of hard and soft palate	Omits all initials	2
62	Hole, 2 by 1 cm., anterior part of palate.....	0	1
63	Hole, 3 by 1 cm., anterior part of palate.....	Omits d 1, 2, 3	1
80	Hole, 1-2 mm., anterior part of palate.....	Indistinct d 1, 2, 3 th 1, 2, 3	2
91	Two holes, 1 by 1 cm. on each side.....	0	2 plus
52	Hole, 1 cm., anterior part of palate; hole, 1 cm., midpalate	t 1, 2, 3 d 1, 2, 3	"hot food sound"
35	Nasal mucous membrane present in arch.....	y 1 omitted	1
69	Abnormal scar	0	1
95	Hole, 1-2 mm., junction of hard and soft palate...	0	1

In one case (80) in which there was a small hole in the anterior part of the palate, the patient articulated d 1, 2 and 3 and th 1, 2 and 3 indistinctly.

From the statistics alone it is rather hazardous to draw conclusions. A defect of the velopharyngeal sphincter was common to all the cases in which there were phonetic defects, but it was also present in a majority of the cases in which phonetic defects were not present. It is the general impression that when a large hole is present in the hard palate, defective closure of the velopharyngeal sphincter is a minor cause of the phonetic defect in spite of the greater constancy of velopharyngeal insufficiency in all of these cases. Omission of the anterior linguopalatals is apparently the more common phonetic defect of large holes of the palate, especially if the holes are in the anterior part of the hard palate or extend into it. Holes in the lateral part of the hard

palate cause a "hot food" quality to be added to the usual nasalization and cause little or no defect in the articulation of the consonants. Small holes in the middle part of the hard palate cause no articulatory dysfunction.

Correlation as Regards Defects of the Soft Palate.—In this analysis there was a hole in the soft palate in only one case (61). This was large, and in spite of nasalization of 2 degrees it probably was the cause of the omission of the initial k and g.

As for the remainder of the cases, the most important factors seemed to be the motility and length of the soft palate. Consequently, in table 6 the cases in which phonetic defects were present are classified according to the length and motility of the soft palate. The number of cases in which the soft palate was of the same motility and length but in which there were no phonetic defects referable to the soft palate are included for comparison.

The relative importance of length, motility and texture of the soft palate as regards closure of the velopharyngeal sphincter was estimated.

The most common defect in this group was omission of soft palate consonants. A certain degree of velopharyngeal insufficiency, as evidenced by the degree of nasalization, was present in every case except one, and in this one there was merely a slurring of k.

There were phonetic defects referable to the soft palate in nineteen of ninety-seven cases in this group. Three cases were not used in this analysis because two belonged in group III, with clefts of the lip and the alveolar process and normal palates, and there were insufficient data on one.

There can be little doubt that the phonetic dysfunction in these cases was dependent almost entirely on the amount of velopharyngeal insufficiency, granting that there was no hole in the soft palate, as in case 61 in which the hole also played an important part.

Relative Importance of Length, Motility and Texture of the Soft Palate in Closure of the Velopharyngeal Sphincter.—Closure of the velopharyngeal sphincter is dependent on the motility, length and texture of the soft palate. Of the patients with soft palates with motility of 4 degrees, 5.8 per cent (one of seventeen) were defective as far as articulation of soft palate sounds was concerned. Of those with palates with motility of 3 degrees, 16 per cent (seven of forty-two) were defective; of those with palates with motility of 2 degrees, 16.6 per cent (three of fifteen) were defective; of those with palates with motility of 1 degree, 28 per cent (four of fourteen) were defective, and of those with palates with no motility, 50 per cent were defective.

Thus, as the motility decreases, the number of cases of defective articulation increase.

As far as length is concerned, 7 per cent of the patients with long palates had defective articulation of soft palate consonants; 17 per cent of those with median palates had this phonetic defect, and 37 per cent of those with short palates were thus affected.

TABLE 6.—*Analysis of Phonetic Defects in Relation to Anatomic Defects of the Soft Palate*

Case	Motility	Texture*	Length†	Nasal- ization	Phonetic Defect	Normal Palates with Same Motility and Length But No Phonetic Defects
17	4	F. S.	M	1	k 1, 2, 3 slurred	
	4	F. S.	L	
	4	F. S.	S	
Total 1						Total 16
14	3	F. S.	L	0	k 1 indistinct	
35	3	F. S.	L	1	k 1; g 1 omitted	
Total 2						Total 12
33	3	F. S.	M	2	k 1, 2, 3 slurred; g 1, 2, 3 indistinct	
21	3	F. S.	M	1	k 1; g	
23	3	F. S.	M	1	k 1, 2, 3 omitted	
90	3	F. S.	M	2	k 1, 2, 3 omitted; g 1 omitted	
Total 4						Total 12
37	3	F. S.	S	1	k 1, 2, 3 omitted	
Total 1						Total 11
60	2	F. S.	M	3	k 1, 2, 3 omitted	
71	2	T. H.	M	1	k 1, 2, 3; g 1, 2, 3 omitted	
Total 2						Total 9
20	2	F. H.	S	2	k 1, 2, 3; g 1, 2, 3 omitted	
Total 1						Total 2
..	2	F. H.	L	
Total 0						Total 4
73	1	T. S.	S	3	k 1, 2, 3; g 1, 2, 3 omitted	
77	1	T. S.	S	1	g 1 = y	
86	1	T. H.	S	1	k 1, 2, 3; g 1, 2, 3 omitted	
67	1	F. H.	S	3	k 1; g 1 omitted	
Total 4						Total 1
..	1	T. S.	M	
Total 0						Total 6
..	1	T. S.	L	
Total 0						Total 3
61	0	T. H.	S	2	k 1; g 1 omitted	
62	0	T. H.	S	1	k 1, 2, 3; g 1, 2, 3 omitted	
78	0	T. H.	S	3	k 1, 2, 3; g 1, 2, 3 omitted	
Total 3						Total 0
..	0	T. H.	L	
Total 0						Total 0
..	0	T. H.	M	
Total 0						Total 3
56	..	T. S.	L	2	k 1; g 1 omitted	
Total 1						Total 0
19						79

* F. S. indicates full and soft; T. S., thin and soft; F. H., full and hard, and T. H., thin and hard.

† L indicates long; M, median and S, short.

As far as length and motility are concerned, one can make no definite statement concerning their relative importance from the statistics alone, but the general impression is that a person with a short palate with good motility has a better chance of good function of the velopharyngeal sphincter than one with a long palate with no motility. An analysis of the whole group of one hundred cases, including those in the group which have just been analyzed, brings this out also. The results show that 50 per cent of the patients with long palates, 69 per cent of those with median palates and 54 per cent of those with short palates had nasalization, while 55 per cent of those with palates with motility of 4 degrees, 62 per cent of those with palates with motility of 3 degrees, 64 per cent of those with palates with motility of 2 degrees, 81 per cent of those with palates with motility of 1 degree and 100 per cent of those with palates with no motility had some nasalization.

Motility seems to be the more consistent as regards the presence of velopharyngeal insufficiency.

As regards the consistency of the soft palate and its effect on articulation, it can be concluded that while it has no effect per se it has an effect secondarily by its relation to motility. The average motility of the full, soft palates is 3; that of the thin, soft palates is 2; that of the full, hard palates is 1.5, and that of the thin, hard ones is 1.1.

Motility is therefore of more importance than length, although the latter is of marked importance for competent closure of the velopharyngeal sphincter. As far as can be determined, little emphasis has been given to possible injury to the nerve supply of the palatal muscles by the different types of operations. No description of the course and distribution of the nerves supplying the tensor veli palatini or the levator veli palatini muscle has been found. It seems of great importance as far as preservation of motility is concerned to demonstrate their course if possible and to ascertain the danger of injuring them in the different types of operation for repair of the soft palate.

Superior Constrictor Muscle.—That the superior constrictor muscle elements are well developed in cases of cleft palate is evident. In this series 88 per cent were classed as well developed. Many of these were apparently hypertrophied, although no definite comparison was made with the normal. The general impression is, however, that the superior constrictor muscle elements are better developed in cleft than in normal palates.

The fact that all repaired cleft palates are as a rule shorter and less mobile than normal palates and yet adequate closure is obtained frequently tends to suggest the importance of this hypertrophy of the superior constrictor muscle for speech.

Importance of the Uvula.—Sixty-one per cent of the patients having long uvulas had some nasalization; 55 per cent of those with median length uvulas were thus affected; 71 per cent of those with short uvulas had nasalization; 78 per cent of those with no uvula were thus afflicted, and 56 per cent of those with bifid uvulas had nasalization.

As there is little consistency in these results, this would tend to show that the uvula is of negligible importance in closure of the velopharyngeal sphincter.

Effect of Adenoidectomy and Tonsillectomy.—That adenoidectomy and tonsillectomy considerably enhance the ability to speak well has often been noted.

One patient (in case 6) was observed before adenoidectomy and tonsillectomy and was seen subsequently one week and again one month postoperatively, and a report from the mother was received three months after operation.

Before operation the result had been classed as excellent. There was no phonetic defect, and the palate had a motility of 3 degrees and was of median length. One week postoperatively the motility and length of the palate were the same, but nasalization of 2 degrees was present. The articulation of the consonants was still good, but the nasalization had changed the quality of the speech markedly. The result of the functional test was poor. One month after operation there was less nasalization (1 degree), less difficulty with the functional test was found and the quality of the voice was improving. Three months after operation, the mother reported "steady improvement" in the speech.

It is impossible to draw conclusions from one case, but it seems reasonable to concede that if a mobile palate of good length is present, tonsillectomy and adenoidectomy can be performed without danger of permanent damage to speech. One feels, however, that if the palate is inadequate as to length and motility in the first place, adenoidectomy or tonsillectomy should not be performed.

Value of Speech Training. Fifty-six per cent of the patients in this series have had no speech training. Twenty per cent have had only occasional corrections by the family. Six per cent have had more persistent corrections by the family. Eight per cent have had occasional lessons in speech. Fourteen per cent have had persistent teaching by well trained teachers.

Fifty one per cent of the fifty six who had had no training were classed as excellent as regards their speech, while 28 per cent had good speech, 20 per cent had fair speech and not one had bad speech.

At the other extreme, only 36 per cent of the fourteen who had had adequate training had excellent speech, 57 per cent had good speech, 7 per cent had fair and none had bad speech.

At first glance, these results would condemn speech training as useless, but a study of the anatomic structures of the two groups brings out the fact that a greater percentage of the patients who have had no training have good anatomic structures, whereas in the group which has had training there is a greater percentage of anatomic defects.

Moreover, as a rule, only the patients with the poorest functional results have been referred for speech training.

There have been several patients who had had speech training, and although they still have a marked degree of nasalization the articulation of the consonants at the stop position is excellent.

Speech training is most important in perfecting correct articulation. It also assists in developing closure of the velopharyngeal sphincter, but with inadequate anatomic material it cannot possibly do this.

Ultimate Speech Result.—Of the one hundred cases presented, the ultimate speech in 42 per cent was classed as excellent, in 43 per cent as good, in 14 per cent as fair and in 1 per cent as bad or unintelligible.

CONCLUSIONS

1. Good anatomic results do not necessarily mean good functional results.

2. Imperfect closure of the velopharyngeal sphincter is by far the most important anatomic element in ultimate speech results.

3. Velopharyngeal insufficiency is the most important factor in the omission, substitution and disarticulation of most of the consonants. The slurring of s and ch is an exception.

4. Velopharyngeal insufficiency is the cause of the nasalization and therefore the disturbed quality of cleft palate speech. There is a possibility that scar tissue and taut mucous membrane play a rôle in the poor quality by disturbing the vibratory capacity of the cavities of the upper respiratory passage.

5. Abnormal contour of the teeth causes slurring of s and ch.

6. Holes just posterior to the alveolar process in the anterior part of the hard palate have a tendency to cause omission of the labiodental consonants.

7. Small holes in the hard palate cause no phonetic defect.

8. Large holes in the middle portion of the hard palate tend to cause a "hot food" quality to speech rather than a disturbance of articulation.

9. Holes in the lateral part of the hard palate tend to cause a "hot food" quality to speech.

10. Holes in the soft palate tend to cause omission of the posterior linguopalatal consonants.

11. The motility of a palate appears to be more important than length as regards closure of the velopharyngeal sphincter.

12. The superior constrictor muscle elements are important in closure of the velopharyngeal sphincter and are usually hypertrophied.

13. The uvula may be of importance in closure of the velopharyngeal sphincter, but the analysis does not indicate this.

14. A person with a cleft palate usually has distorted nasal cavities, and occasionally the inferior turbinate bones are enormously dilated.

15. Adenoidectomy and tonsillectomy are indicated if the motility and length of a palate are good.

16. Speech education is of greatest value in correcting articulation.

17. No amount of education will entirely overcome marked velopharyngeal insufficiency, although it is of definite value in lesser degrees of insufficiency.

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PYOGENIC OSTEOMYELITIS OF THE PELVIS

ANALYSIS AND DISCUSSION OF NINETY CASES

J. KULOWSKI, M.D.

ST. JOSEPH, MO.

This study demonstrates the essential similarity of pelvic osteomyelitis to the more common osteomyelitic manifestations in the long bones. However, pelvic localization is distinguished by its anatomic situation, as defined by the peculiar developmental configuration of the innominate bone and its relation to the adjacent fascial spaces, viscera and the hip joint. These features anticipate the differential diagnostic problems encountered. It is characteristic of the disease that the primary lesion is overlooked or subordinated to the predominant simulative signs and symptoms or to the more extensive secondary parosteal purulent infiltrations. Therefore, pyogenic osteomyelitis of the pelvis continues to challenge diagnosis and treatment during its earlier, more favorable stages, although it is a relatively common devastating disease.

In a series of 1,496 cases of pyogenic osteomyelitis, there were 90, or 6 per cent, in which the focus of infection was in the pelvis. This lesion was third in the order of relative frequency. The ratio (table 1) of males to females in the group of 90 cases was approximately 2:1, except in the group in which the infection was in the sacro-iliac region. The age range was from 2 to 63 years, with an average age of 16 years. Pelvic osteomyelitis is primarily a disease of the growing period. The majority of cases (about 60 per cent) occurred in the second decade. Because of the relation of the sacro-iliac region to spinal foci, there is a relative increase in the later decades.

PATHOGENESIS (TABLE 2)

The apparent port of bacterial entry could be determined in 20 instances. In 17 it was a topical infection and in 3 an acute infectious disease. Boils were the predominant localized infection of the skin. The relationship between such ports of entry and the osteomyelitic process is not always clearcut. Adequate treatment of all topical focal infections, as well as of acute infectious diseases, is an important prophylactic measure. Antecedent trauma was recorded in 35 cases. In most of these the onset of symptoms followed direct or indirect injury,

From the University Hospitals at Iowa City.

Services of Drs. A. Steindler and H. L. Beye.

sometimes dramatically so. The crests of the ilium are not well protected by the soft parts. The sacro-iliac joints are notoriously prone to indirect strains. The ischium and the pubis are readily injured by falls on the buttocks and especially by straddling. The relationship between antecedent trauma and pelvic osteomyelitis substantiates the time-honored assumption of its etiologic importance.

Pelvic osteomyelitis may be classified as a direct or a hematogenous infection. The former follows gunshot wounds, operations and compound fractures or is due to extension from a neighboring suppurative process and infected decubiti. There were 23 (about 26 per cent) cases of direct infection. In 2 cases sacro-iliac osteomyelitis followed arthrodesis, in 1 it was due to extension from an iliac osteomyelitis and in 7 it was associated so closely with disease of the lumbosacral region as

TABLE 1.—*Sex and Age Incidence in Ninety Cases of Pyogenic Osteomyelitis of the Pelvis*

	Ilium	Sacro-Iliac Joint	Ischium	Pubis	Total
Sex:					
Males.....	20	22	14	6	62 (68%)
Females.....	11	7	7	3	28 (32%)
Age, years:					
Youngest.....	4	5	2	4	3
Oldest.....	63	50	33	59	51
Average.....	16	21	11	16	16
Decades:					
1.....	5	2	0	3	19 (21.11%)
2.....	21	19	10	3	53 (58.88%)
3.....	1	1	1	1	4
4.....	2	1	1	1	5
5.....	1	5	0	0	6
6.....	0	1	0	1	2
7.....	1	0	0	0	1

to preclude initial localization. In 4 cases iliac osteomyelitis was due to extension from the initial lesion of the hip, and in 1 it resulted from an infected compound fracture. In the 4 cases of ischiac osteomyelitis the condition originated from primary foci of the hips. In 1 case pubic osteomyelitis occurred after a simple fracture, which was operated on and fixed by wire; in 2 it followed pelvic fracture and was associated with genito-urinary complications, and in the fourth it was due to a dissecting superficial abscess of the groin.

Sixty-seven (74 per cent) of the cases of pelvic osteomyelitis were of the hematogenous form; the lesions in 55 were initial, and in 12, metastatic after the establishment of a bony focus elsewhere. On the basis of the predilection of pyogenic osteomyelitis for growth zones, a diphasic clinical syndrome may be observed as a general rule, corresponding to the two periods of bony development. The first period extends from infancy to puberty, at the end of which period the three bones composing the acetabulum fuse. The second period commences

with the ossification of the acetabulum and the appearance of the marginal epiphyses and extends to the time of fusion of the marginal epiphyses, at about 25 years of age. The first period is characterized by a more diffuse lesion, almost invariably occurring at the border of the acetabulum. The second period localizes about the marginal epiphyses. In the sacro-iliac region the initial process begins most commonly on the sacral side but may originate in the ilium or the joint proper. Very soon, however, the entire joint is involved.

Staphylococcus was recovered in the great majority of instances. Sterile cultures are also significant, since the organism may be in the bone and not free in the exudate. Sterile cultures always indicate a most careful laboratory search to rule out tuberculosis, a malignant process or some unusual bacterial invader. The mixed forms are secondary invaders for the most part. Careful initial blood and local cultural studies reveal not infrequently the presence of several organisms, which

TABLE 2.—*Pathogenic Classification of Cases of Pelvic Osteomyelitis**

	Ilium	Sacro-Iliac Joint	Ischium	Pubis	Total
Direct infection.....	5	10	4	4	23 (25.55%)
Hematogenous infection					
Primary lesion.....	20	16	15	4	55 (61.11%)
Metastatic lesion.....	6	3	2	1	12 (13.33%)
Infectious agent					
Staphylococci.....	12	14	12	4	42
Streptococci.....	3	2	0	0	5
Mixed infection.....	2	2	1	0	5
Sterile culture.....	1	4	0	1	6
Positive blood culture.....	4	2	4	0	10

* Possible ports of bacterial entry and antecedent trauma play an important rôle in the apparent pathogenesis in this series. The latter was recorded in 35 instances of the disease in the following sites: sacro-iliac joint, 12; ilium, 8; ischium, 11, and pubis, 4. There were 17 recorded instances of previous topical infections, which occurred as follows: sacro-iliac joint, 6; ilium, 5; ischium, 5, and pubis, 1. There were 3 instances of previous acute infectious diseases: sacro-iliac joint, 1, and ilium, 2.

are apparently simultaneous primary bacterial invaders. Most frequently there is recovered a combination of staphylococci and streptococci. A positive blood culture yielding staphylococci or streptococci is of considerable differential diagnostic importance.

PATHOLOGIC ANATOMY (TABLE 3)

There were 4 cases in which the lesions were bilateral, all of which proved to be fatal; in 3 the sacro-iliac joints and in 1 the ischiums were involved, making a total of 94 foci. The cases of bilateral sacro-iliac osteomyelitis were associated with involvement of the lumbosacral region, and the cases of ischiac osteomyelitis, with extensive hemipelvic disease. Pelvic localizations are all more or less diffuse, owing to the peculiar bony configuration and the tendency to chronicity, especially after obliteration of cartilaginous barriers. Seventy per cent were associated with other segmental foci, chiefly by extension. The hip joint is the most frequent site of an associated focus.

The most striking pathologic feature of pelvic osteomyelitis is the relatively "dry" bony reaction as a subacute or chronic fibrous type of osteomyelitis. Conversely, extensive suppuration of the soft tissue is characteristic. The fibrous reaction is partly due to collateral ischemia. The initial site of involvement usually reveals a more active inflammatory reaction. Sequestration is not as uncommon as the literature would indicate. The preponderance of cancellous bone, negligible marrow cavity and excellent circulation is inducive to caries rather than to necrosis. In the sacro-iliac region sequestrums are small and usually situated antero-inferiorly. The changes in the joints are the same as those of infectious arthritis elsewhere. The thin cortical bone of the iliac wing leads to early perforation and variable-sized sequestrums, especially on its pelvic surface. Consequently, it is common to observe at operation the formation of large irregular cisterns on the pelvic surface of the bone, which are filled with pus, sequestrums and débris

TABLE 3.—Pathologic Anatomy in Cases of Pelvic Osteomyelitis

	Ilium	Sacro-Iliac Joint	Ischium	Pubis	Total
Unilateral osteomyelitis.....	31	26	20	9	86
Bilateral osteomyelitis.....	0	3	1	0	4
Extensive lesion.....	17	20	13	3	53 (58.88%)
Localized lesion.....	14	9	8	6	37 (41.12%)
Associated extension					
Pelvic lesions					
Hip.....	13	5	7	1	26 (44%)
Ilium.....	..	7	3	..	10
Ischium.....	3	1	4
Pubis.....	1	..	4	..	5
Lumbosacral portion of spine....	..	8	8
Sacro-iliac joint.....	6	6
	23	20	14	2	59 (70%)

(fig. 12). Occasionally the entire wing is converted into a variegated necrotic mass. At operation in the later stages of the disease the ischium lies in a soggy bed and can be lifted out *en masse*.

A striking feature of the later stages is the amount and irregularity of new bone formation. The periosteum is very active in cases of pelvic osteomyelitis, and the tendency toward regeneration—even after total resection—is almost certain in the young. This regenerative irregularity often adds to the operative difficulties encountered. The power of the periosteum may be weakened or inhibited entirely in older persons or because of constitutional inferiority, initial thrombosis and death of the periosteum or intense parosteal infection. Necrosis and intense edema of the surrounding soft parts may predominate the situation. Even in the early stages the histologic tendency toward thickening and eburnation of the bony lamellae is conspicuous.

COMPLICATIONS (TABLE 4)

The complications of pelvic osteomyelitis especially reflect the clinical life history. The dovetailedness of these phenomena reveal an apparent

harmony, imperceptible from any other perspective. It is now evident that most complications are of surgical interest, since the vast majority are dependent on the local skeletal lesion. Table 7 indicates this clearly.

Suppuration was observed in over 83 per cent of this series and largely determined the course of the disease. These abscesses tend to gravitate and accumulate in the anatomically related fascial spaces of the thighs, the lower part of the back and the gluteal regions, which are easily invaded. Such purulent collections predominate the surgical situation not alone because of their complexity and bulk but because their shaggy infiltrated walls become in themselves formidable sources of local and systemic infection.

The possible pathways taken by pus originating in the sacro-iliac joint after it has perforated anteriorly illustrate the ramifying tendencies of all pelvic lesions. Pus may follow along the iliopsoas muscle to the inner aspect of the thigh or along the pectineus muscle posteriorly; it may enter the hip joint via a bursa found between the iliopsoas tendon and the anterior part of the joint, or it may burrow posteriorly along the obturator internus muscle or along the pyriformis muscle as a low gluteal abscess or upward from the iliac fossa into the lumbar region. Abscesses arising from iliac foci are of special interest because of their relation to the inner surface of the bone, which is divided by the iliopectineal line into an upper, expanded, portion and a lower, smaller, part. The iliac fossa above and anterior is smooth by sloping, which explains the great prevalence of abscess formation in this region and its tendency to point anteriorly in Scarpa's triangle; since pus is blocked from passing farther into the true pelvis by the structures attached to the iliopectineal line, gravity forces it forward rather than backward. Infected compound fractures of the pubic bones are especially interesting because of the relationship of the bladder and the posterior portion of the urethra. An extensive abscess in the space of Retzius was observed in 1 case in which the pyogenic infection was associated with traumatic rupture of the posterior portion of the urethra. Suprapubic cystotomy and perineal urethrotomy were performed, and the patient died after a stormy course of three weeks' duration.

CLINICAL ANALYSIS (TABLE 5)

In a general way the onset of the disease determines whether the local or the systemic reaction will dominate the initial clinical stages. The disease becomes chronic in practically all survivors, as shown by the average duration of symptoms in this series. The paucity of recorded clinical dates emphasizes the unsuspected nature of the disease in many of these cases. There are, however, sufficient facts obtained to indicate the general clinical picture. It should also be remembered that rather

extensive destructive lesions of a low grade nature may present few or no symptomatic clues. In retrospect, it is evident that a knowledge of the disease is of primary importance for a reasonably early diagnosis.

DIAGNOSIS

The chief differential diagnostic interest centers about the hip joint. However, this also involves a discussion of a wide variety of other

TABLE 4.—*Complications in Cases of Pelvic Osteomyelitis*

	Ilium	Sacro-Iliac Joint	Ischium	Pubis	Total
Suppuration.....	27	21	18	9	75 (83.33%)
Pelvic.....	15	10	2	1	28 (37.33%)
External.....	7	4	11	3	25 (33.33%)
Thigh.....	5	7	5	5	22 (29.44%)
Flare-up.....	13	17	7	3	40 (44.44%)
General sepsis.....	12	15	5	5	37 (41.11%)
Spontaneous sinus.....	9	11	7	2	29 (32.22%)
Deformity.....	15	4	6	1	26 (28.88%)
Skeletal metastasis.....	9	6	7	1	23 (25.55%)
Sequestrum formation.....	11	4	4	2	21 (23.33%)
Vascular complications.....	2	2	4
Decubiti.....	1	2	3
Amyloidosis.....	..	2	2
Rectal perforation.....	1	..	1	..	2
Peritonitis.....	1	1

TABLE 5.—*Clinical Analysis of Cases of Pelvic Osteomyelitis*

	Ilium	Sacro-Iliac Joint	Ischium	Pubis	Total
Onset					
Acute.....	13	11	9	5	38
Subacute.....	7	7	5	4	23
Chronic.....	6	3	2	..	11
Duration, months					
Shortest.....	0.15	0.3	0.1	0.1	0.16
Longest.....	676	84	276	132	202
Average.....	47	27	34	35	33
Symptoms					
Subjective					
Pain localized.....	7	10	4	4	25
Pain referred.....	9	10	6	2	27
Objective					
Local tenderness.....	8	10	10	3	31
Muscle spasm.....	3	3	..	1	7
Loss of weight.....	9	8	3	4	24
Superficial abscess.....	8	3	6	3	20
Pelvic abscess.....	5	6	..	2	11
Edema and infiltration.....	5	6	6	1	19
Deformity of hip.....	10	13	7	..	31

extrapelvic lesions, such as inflammation of the lower part of the abdomen and pelvis, spondylitis of the lumbar and lower part of the dorsal region, subgluteal bursitis, ischio-rectal abscess, isolated abscess of the iliopsoas muscle and bursitis, as well as malignant lesions and tuberculosis. Ruling out actual involvement of the hip joint offers the greatest clinical obstacle to a reasonably early diagnosis, since a sympathetic juxta-articular effusion occurs so frequently. It should be remembered

in this connection that the joint may be the primary seat of infection, be affected simultaneously or included in the process by extension secondarily. Marked symptoms referable to the hip joint, especially when accompanied by radiating pain along the internal obturator nerve, are almost pathognomonic of relative or absolute participation of the hip joint in the disease.

Primary disease of the hip joint is early associated with more or less of a position of instability of the joint, mainly flexion, abduction and external rotation. The flexed position may be combined with adduction and internal rotation. This position is conditional on the relationship of the initial localization of the infection to the anatomic quadrants of the acetabulum, the head of the femur or the pelvifemoral musculature. Thus the resultant subsequent position of the hip is maintained by a specifically activated protective muscle spasm pattern characterized by relative or absolute spasm. However, some degree of motion may be elicited before the joint cartilage is involved, or in the more chronic lesion due to the capsular and ligamentous relaxation incident to a prolonged state of hydro-arthrotic distention. When the disease is in the pelvis, the attitude of the hip and the limitations of joint motion are less significant. Extra-articular conditions will allow a considerable range of motion in the joint in the planes not controlled by those pelvifemoral muscles arising or inserting at sites of bony involvement. Therefore, the attitude of the hip is now sympathetic and relatively atypical. When the focus is in the ilium, the hip is characteristically in flexion and abduction. Flexion predominates when the focus is in the sacro-iliac joint. When the infection is localized in the ischium, external rotation of the femur is present. If the disease is in the pubis, there follow flexion, adduction and internal rotation as a rule.

Aspiration of the hip joint and surrounding structures is the most important single factor in the clinical evaluation of suppurative localizations. This must be persisted in intelligently and may be performed with the patient under general anesthesia. The gross and laboratory examinations of the material withdrawn yield the key to the situation.

Special emphasis should be given to the infection in the sacro-iliac region, since it involves the syndrome of pain low in the back. It may be impossible to make a differential etiologic diagnosis without exploration and biopsy. Even so, the laboratory tests were misleading in several cases in that the exudate yielded a positive reaction when injected into a guinea-pig, but the reaction was not substantiated by subsequent autopsy examination or pathologic studies of sufficient material removed at operation. Disease of the sacro-iliac joint often simulates disease of the hip joint. On examination the motions of the hip will be free, except the extremes of flexion and extension, because the former puts tension on the hamstring muscles, which is transmitted to the sacro-

iliac joint, and in sacro-iliac involvement the latter is restricted by associated spasms of the iliopsoas muscle. It is most difficult to differentiate sacro-iliac osteomyelitis from sacro-iliac tuberculosis. Ombredanne considered the latter to be rare in infancy, and Wilmath stated that it is exceptional before the age of 20. In children the tuberculous process of the os ilium originates at some distance from the bone as osteomyelitis. It is more rapid in the adult and is primarily an involvement of the joint or osteo-arthritis. The initial reaction may, however, be ushered in by a septic fever or the appearance of a tuberculous focus in other places. In the adult type of sacro-iliac tuberculosis in the early stages there are five symptoms of value: sacroradiculitis, painful limp, sacro-iliac diastasis (noted roentgenographically) and upward displacement of the pubic bone and, finally, localized surface and rectal tenderness, elicited digitally.

Abdominal and pelvic inflammations are simulated chiefly by localizations of the disease in the sacro-iliac joint and in the ilium, especially in the latter. In the acute stages the profound general reaction and bacteremia point toward pyogenic skeletal disease. Careful observation of spontaneous and of provoked pain is a great aid in the diagnosis. Spasm of the abdominal muscles, when present, confines itself to the iliac crest and soon takes on the character of induration and even of edema. This tenderness even very early may be outlined in the posterior portion of the ilium along the crest or even may simulate a perinephritic abscess. Tenderness is common in the groin but cannot be accurately limited. When perforation occurs, the temperature and the general condition are improved. Some pain persists, however, and soon a purulent collection in the pelvis is clinically evident. In acute pubic lesions one has to distinguish between phlegmonous inflammation in the space of Retzius, suppurative arthritis, psoasitis and myositis of the rectus abdominalis muscle. Ischiac lesions offer no particular difficulties if the examiner thinks of the possibility.

ROENTGENOGRAPHIC EXAMINATION

The roentgenogram is indispensable for diagnosis and proper surgical evaluation, particularly in the subacute and chronic stages of the disease. The entire pelvis and the lumbar portion of the spine must be carefully checked after the patient has been properly prepared. Several pronounced lesions of the iliac wing were missed early in the series because of failure to observe this simple detail. Lateral views of the iliac bones and hips are helpful, since localized lesions of the ilium can be visualized even early. Although the general operative risk determines the surgical indication, no operative procedure can be intelligently planned without a complete preliminary roentgenographic study of the

situation. The changes in the soft tissues are of some significance in the early stages of acute inflammatory conditions and are observed as capsular and other fascial and muscular distortions and infiltrations. In cases of ischiac lesions the obturator foramen may be clouded early because of abscess formation. The hip joints must be extended if possible to avoid superimposed shadows from the tissues of the thighs. The essential changes depicted by the roentgenogram are osteoporosis, sequestration and bone production. Osteoporosis is the earliest sign in the acute stage. Its delay is due to the fact that the calcium salts early remain at the site of involvement in an attempt to limit the pathologic process. It appears soonest in the more primitive cancellous portions of the bones in which calcium is not so bound up as in the more highly organized haversian architecture prevalent in cortical bone. Because osteoporotic changes sometimes persist, these lesions simulate tuberculosis and even malignant processes. Except in the pubis and the sacro-iliac region, the regenerative features are characterized by great thickening and irregularity. In the chronic phases there is left a mass of irregular sclerotic thickened periosteal bone with little or no architectural detail that can be made out. The value of injection of a sinus with a radiopaque substance cannot be overemphasized as an aid to diagnosis.

END-RESULTS (TABLES 6 AND 7)

The inadequacy of treatment previous to hospitalization reflects the general attitude of the medical profession toward this disease. These lesions have always been considered as hopeless and attended by a grave prognosis. Of the 29 cases of sacro-iliac lesions, the superficial abscess was incised in 7 and aspirated in 2. Of the 21 cases of ischiac osteomyelitis, incision was performed in 5 and curettement in 1. Of the 21 cases of iliac lesions, curettement was performed in 4 and simple incision in 4. The pubic lesions were not treated. The treatment in the hospital also indicates an absence of definite principles in the earlier cases. On the whole, the best results were obtained after the need for more adequate treatment was recognized.

Of the 18 cases of sacro-iliac osteomyelitis in which the bone was attacked, curettement was done posteriorly in 5, and the Smith-Petersen technic was used in 5, total resection in 3 and partial resection in 5 (1 bilaterally). The Smith-Petersen technic is adequate for circumscribed lesions, especially when reenforced by Orr's postoperative routine. In 1 case this procedure was followed by total resection at a later date. In the second case two further operations were necessary. In 2 the lesions were not suppurative, and in the fifth a subgluteal abscess developed one month after operation. In 7 cases simple incision and drainage were employed, the only favorable result being obtained

by the Orr method. There was no operative mortality in the group in which resection was done. Three patients died subsequently from complications already present at the time of operation. In 5 cases healing occurred in from six months to one year.

In the group of patients with iliac osteomyelitis there were 2 adolescents (1918 and 1927) who were treated by roentgen irradiation, with apparent cessation of the clinical symptoms. Five of the patients

TABLE 6.—*Treatment and End-Results in Cases of Pelvic Osteomyelitis**

Type of Treatment	End-Result	Ilium	Sacro-Iliac Region	Ischium	Pubis	Total
Radical.....	Healed	7	13	4	2	26
	Died	1	3	2	1	7
	Unknown	2	2	2	0	6
Incision.....	Healed	1	1	2	1	5
	Died	3	1	1	0	5
	Unknown	9	3	3	3	18
Conservative.....	Healed	4	1	0	0	5
	Died	0	0	1	1	2
	Unknown	4	5	6	1	16

* This table classifies the treatment as a whole. Radical treatment indicates that the affected bone was attacked in one way or another. The affected bone was not attacked at all in the cases included under simple incision. Conservative treatment includes roentgen irradiation, the use of casts or other mechanical methods, simple hospitalization or no active treatment at all. The mortality as regards the cases as a whole is: radical treatment, 18 per cent; incision, 18 per cent, and conservative treatment, 9 per cent. However, on the basis of the cases in which the end-results were known the mortality is as follows: radical treatment, 21 per cent; incision, 50 per cent, and conservative treatment, 40 per cent.

TABLE 7.—*End-Results in Unselected Cases of Pelvic Osteomyelitis in which Resection Was Performed*

Localization	Operation	Number of Cases	Healed	Died	Mortality
Sacro-iliac joint.....	Partial resection	5	3	2	40%
	Total resection	3	2	1	33.33%
Ilium.....	Partial resection	4	3	1	25%
	Total resection	1	1	0	0
Ischium.....	Total resection	4	4	0	0
		17	13 (76.48%)	4	23.52%

were not treated for one reason or another. Three were treated by sequestrectomy without success. Thirteen were treated by simple incision and drainage; healing occurred in 1, and 3 died. Of the more radical procedures, total resection was performed once, partial resection four times, saucerations several times and trephination once. In the case in which trephination was done over 50 metastatic foci subsequently developed. There was only 1 death in this group.

Simple incision and drainage were performed in 6 cases of ischiac osteomyelitis, with cures from well circumscribed foci in 2. The disease was bilateral in 1 of the remaining 4 cases, and it extended to the hip

in 1 and to the ilium in the other. In the fourth case the condition proved fatal. Death also occurred in the 2 cases in which sequestrectomy was performed and in 1 case in which a simple incision was done. In another case a mistaken diagnosis of disease of the hip joint was made, and operation was performed, with fatal results. The radical operations (resection) were performed in the acute and subacute stages of the disease with sound healing within from three to six months.

In the 5 cases of direct infection of the pubic bone, simple incision and drainage were employed. Autopsy in the fatal cases revealed a huge abscess in the space of Retzius, which extended laterally into the iliac fossae. The metastatic focus in the cases of hematogenous infection drained spontaneously. Sequestrectomy was performed on a boy two weeks after onset, with healing in four months. Simple incision on a 4 year old girl, three weeks after an acute onset, ended in extension of the lesion and death. A youth aged 17 years was treated by a cast, with subsequent invasion of the anterior compartment of the thigh. The most gratifying and convincing result followed prompt adequate treatment in a case of acute involvement in which the abscess and involved bone were treated by the Orr method.

TREATMENT

The need for radical treatment was recognized and urged by the earliest writers on iliac lesions. Perhaps their very zeal delayed the acceptance of these principles. An extended experience with pyogenic osteomyelitis supports this fundamental therapeutic truth relative to established foci of the disease. One should remember that the lesion may be nonsuppurative and that spontaneous healing may occur. However, pelvic osteomyelitis is essentially a most devastating disease which demands bold operative measures. The key to the individual situation is revealed by the complications of the disease in general. The vast majority of these depend primarily on the skeletal lesion and only secondarily on any existing systemic reaction. Therapy now resolves itself into the primary and secondary control of the disease.

Primary control of the disease involves the initial systemic infection and the determination of the local suppurative focus. These must be considered in the order of their appearance. Henceforth the most aggressive measures continue to be directed against whichever predominates the clinical situation. Until contradictory knowledge affecting the relationship between the port of bacterial entry, the systemic infection and the local lesion is attained, adequate drainage is indicated when localization is clinically established. Pyogenic osteomyelitis anywhere is not a surgical problem until this occurs. The successful termination of the acute stages of the disease depends on the surgeon's experience

with the disease. Therefore, treatment at the onset must be directed against the systemic situation by the several means at one's command—dextrose solution intravenously, small repeated transfusions, sedatives, splinting, traction or casts—and one should ever be on the watch for localizing skeletal signs and symptoms. Perhaps early diagnosis and immediate bony drainage have been overemphasized at the expense of a careful evaluation of the surgical risk. The fault rests with the individual surgeon. Poor preoperative surgical judgment reflects unfairly on and discredits sound axiomatic principles of drainage. However, the conservative postoperative technic of Orr permits more extensive surgical treatment in the early stages than would otherwise be feasible in pelvic localizations of the disease.

As a rule the signs of localization in the soft tissue appear within a few days of the onset of symptoms. Simple incision and drainage will suffice until more definite pathologic skeletal delineation is manifest. By this time the operative risk and the operability of the lesion will determine all further operative details. Wide excision of affected bone is the ideal to be attained. Several factors are effective indicators of improvement of the patient's operative risk and of definite establishment of localization of the disease: a decrease in the initial rapidity of the sedimentation rate, intermittent fever after an initially sustained level of temperature, associated with a lowered pulse rate, a fair cellular blood level and even diminished apprehensiveness and pain.

Secondary control of the disease is based on anticipation of pathologic extension, sequestrum, secondary infection, persistent sinus and flare-ups and above all on locomotor disturbances. The patient now definitely becomes a veritable battleground between the conscientious surgeon and complications, which are practically all preventable or amenable to treatment. Extension of the disease involves chiefly the adjacent joint or joints and the fascial spaces and their contents. Sinus formation enhances secondary infection or even malignant change. Locomotor disturbances are caused principally by deformities of mechanical origin. All of these can also be most uniformly prevented by observing Orr's second great principle, that of adequate rest of the parts.

Pelvic osteomyelitis adapts itself to radical treatment in spite of the apparent complexity of the anatomic situation. The peculiar anatomic structure of the bony pelvis permits a diffusion of functional stresses for its weight-transmitting function through its posterior and anterior arches. The complexity of the soft tissue elements of the pelvis is compensated for by the ready subperiosteal surgical exposure of the bony segments.

The irregular structure of the innominate bone is dissipated when it is regarded as a figure 8 twisted on itself. The acetabulum is there.

fore situated at the isthmus. The upper two-fifths forms the ilium; the ischium comprises the lower and posterior two-fifths, and the pubis, the remaining one-fifth. The fairly even distribution of the parts is not generally appreciated. The thicker parts of the iliac bone consist of cancellous tissue enclosed within two layers of compact tissue, which are lined by periosteum. The thinner parts of the bottom of the acetabulum and the center of the iliac fossa are transparently thin and composed entirely of compact tissue. The inner surface of the ilium is of interest in relation to pyogenic infection. In general, the ischium is the posterior and inferior portions of the lower expanded part of the innominate bone and helps to form the posterior boundary of the obturator foramen. The body is the lower two fifths of the acetabulum and spine of the ischium and is limited below by its neck. The posterior border of the neck is the lesser sacrosciatic notch. The tuberosity of the ischium continues down from the neck to the ascending ramus and forms the rocker of a rocking chair. It is triangular in cross-section. The ascending ramus is a thin plate of bone going up to meet the descending ramus of the pubis. These two pubic bones complete the pelvic girdle and consist of a body and a descending and an ascending ramus. The descending ramus meets the ischium and completes the boundary of the obturator foramen. The ascending ramus goes laterally from the body and upward to end in the acetabulum. The body is the portion at the symphysis and has a quadrilateral form. Its upper border is thicker than the lower.

The sacro-iliac joint is a true joint cavity and has a synovial lining, which is supported by a capsule. The joint surfaces are ordinarily smooth, save for sufficient roughening to lock the joint surfaces. The lumbosacral cord lies directly over the lower third of the sacro-iliac joint. In this region nothing except the joint capsule intervenes between the nerve trunk and the joint space. The proximity of the superior gluteal vessel to the inferior margin of the greater sciatic notch offers a real danger during resection of the sacro-iliac joint and ilium. Enormous superior gluteal arteries, often the size of a man's thumb, have been found in cadavers. The vessels are separated from the ilium only by the periosteum. They are about 1 inch (2.5 cm.) long and have a tendency to retract into the pelvis when severed. Other structures in close proximity to the anterior portion of the sacro-iliac joint in the pelvis that are of surgical importance are the great pelvic vessels, the ureters, the lumbosacral plexus and the rectum. The rectum forms at the third sacral segment and accommodates itself to the hollow of the sacrum and the coccyx. All of these are more or less protected by the iliopsoas structures, which are further thickened by inflammatory edema and infiltration when the sacro-iliac joint is involved by osteomyelitis.

The sacro-iliac joint and adjacent structures are attacked by the Bardenheuer-Picque technic.

In resection of the ilium a Smith-Petersen incision permits the entire external soft tissue flap to be stripped down to the margin of the acetabulum and is followed by anterior deep dissection to expose the anterior portion of the ilium. Posteriorly, the exposure continues to the greater sciatic notch. Next a similar subperiosteal exposure is made of the internal surface of the ilium. At this stage it is remarkable to note how the abdominal contents fall away to complete the exposure of the wing of the ilium down to the arcuate line of the ilium. In cases of chronic involvement subperiosteal dissection will be somewhat difficult because of scarring due to perforation and the formation of an involucrum. One may then remove the ilium as indicated or *en masse* to the supracotyloid region.

My technic for resection of the ischium employs a posterior vertical or transverse gluteal approach, because it is adequate, is farther from the anal canal, furnishes a thick soft tissue pad for subsequent healing and does not require any unusual position of the patient. An incision of from 4 to 6 inches (10 to 15 cm.) long is made over the lateral margin of the tuberosity of the ischium. The dissection continues to the tuberosity. The lowermost fibers of the gluteus maximus fibers are encountered and may be retracted upward or incised near their lower origin. Next the sciatic nerve is located lateral to the tuberosity, freed and retracted lateralward and slightly upward with the fibers of the gluteus muscle. The periosteum and ligamentous attachments of the tuberosity are now boldly incised to the bone between the medial and the lateral hamstring muscles and the external rotator muscles of the hip. Subperiosteal stripping continues upward and downward as far as is necessary to remove all the involved bone. One can proceed to the acetabulum or to the pubis. The stripping is enhanced because of the thickening and edema of the periosteum usually present in osteomyelitic foci. No important structures are jeopardized if the dissection is continued strictly to the subperiosteal region, as these are all lifted away medially and laterally with the basic periosteal flaps. The bone can be removed piecemeal with the curet or rongeur or severed with a saw or mallet and chisel. In extensive lesions the entire bone may be lifted out of its bed. With ordinary care in sealing off the wound, rectal contamination does not occur. The patient may be constipated for several days after operation by the administration of opium.

REPORT OF CASES

Osteomyelitis of the Sacro-Iliac Joint.—CASE 1.—L. B., a white boy aged 15 years, was admitted to the hospital on Dec. 16, 1931, with symptoms of six weeks' duration. The condition began suddenly, with headache, chills, fever and a dull

aching, nonradiating pain "back of the right hip," soon accompanied by diarrhea and urinary frequency. Objectively, there was fulness in the right lower abdominal quadrant. Moderate swelling and tenderness were noted over the right sacro-iliac region. Digital rectal examination revealed a tender fluctuating mass at the lower margin of the right sacro-iliac joint. The white cell count was 14,200. Roentgen examination confirmed the destructive nature of the sacro-iliac and the adjacent iliac lesion (fig. 1). A diagnosis of pyogenic osteomyelitis was made.

Operation.—Total resection of the sacro-iliac joint was done in January 1932. The periosteum of the ileum was found to be thickened, gelatinous and of a dirty grayish color. The bone beneath was injected and roughened. At the junction of the middle and the posterior third of the ilium, just below the crest on the pelvic surface, there was encountered a sequestrum measuring about 3 inches (7.6 cm.) in diameter. It lay loosely in a subperiosteal crater of pus and debris. Thick pus was present in the anterior part of the joint as well as another sequestrum. Most of the sacrum was necrotic, and considerable curettage was necessary to reach healthy bone. The immediate postoperative convalescence was uneventful.



Fig. 1 (case 1).—Roentgenogram showing sacro-iliac osteomyelitis with sequestrums in the anterior margin of the joint and the posterior wing of the ilium. There is slight asymmetry of the pelvis.

The temperature was normal two weeks after operation. *Staphylococcus aureus* was recovered. The diagnosis in the pathologic report was pyogenic osteomyelitis. Complete healing occurred in about eighteen months.

CASE 2.—R. C., a white man aged 21, was admitted to the hospital on Sept. 23, 1931, with symptoms of ten days' duration, which were of sudden onset, with a dull aching pain in the left groin, painful micturition and fever. The patient appeared acutely ill and septic. The left inguinal glands were enlarged and tender. A tender soft mass could be palpated in the lower part of the left side of the pelvis. There was suggestive tenderness over the left sacro-iliac region. A roentgenogram revealed blurring and increased condensation about the sacro-iliac joint. The white cell count was 16,500. General hygienic measures and traction were continued for several weeks until the diagnosis of pyogenic osteomyelitis was more certain and the operative risk less.

Operation.—Partial resection was done. The sacral portion was markedly necrotic. About 500 cc. of pus was evacuated from the pelvis. There was a moderate degree of shock. *Staph. aureus* was recovered, and inoculation of a

guinea-pig gave negative results. The diagnosis in the pathologic report was pyogenic osteomyelitis. The convalescence was uneventful, except for several metastatic abscesses in the soft tissue. Healing occurred in ten months (fig. 2 *B*).

CASE 3.—D. T., a white youth aged 17, was admitted to the hospital on Jan. 18, 1933, with symptoms of four months' duration, consisting of pain in the back and sciatica of acute onset. He had lost 28 pounds (12.7 Kg.) in weight. Two weeks before operation a spontaneous sinus appeared over the left buttock. There was bilateral spasm of the lumbar muscles, which, however, permitted considerable spinal motion. There was definite tenderness over the left sacro-iliac joint. The motions of the hip were free. The white cell count was 11,400. A roentgenogram showed a destructive lesion of the left sacro-iliac joint. A diagnosis of pyogenic osteomyelitis was made.

Operation.—Total resection was done. The chief destruction was found in the upper and anterior poles of the joint, involving the sacrum considerably. The

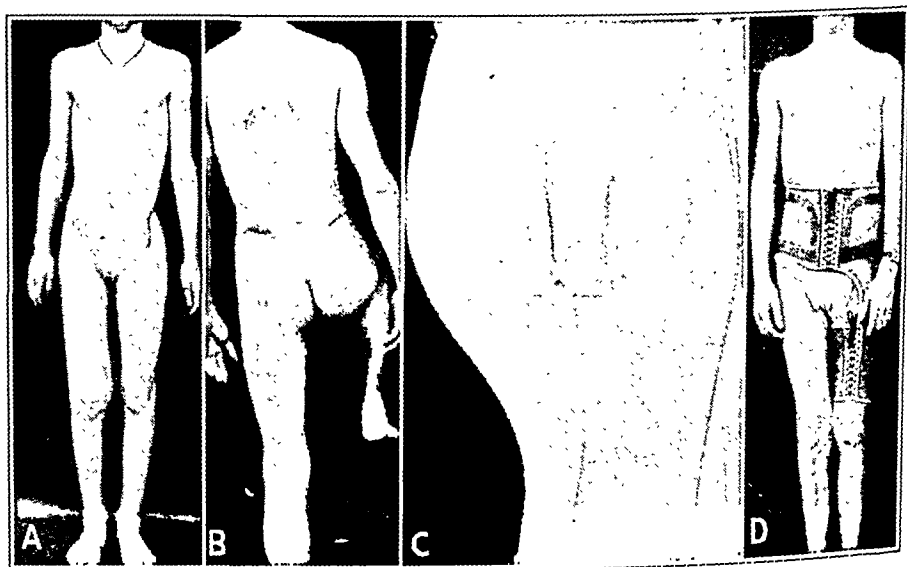


Fig. 2.—Photographs of patients in whom healing has occurred. *A* (case 10) shows a patient with healed osteomyelitis of the ilium; *B* (case 2), a patient with healed osteomyelitis of the sacro-iliac joint, demonstrating a negative reaction to the Trendelenburg test; *C* (case 15), a patient with healed osteomyelitis of the ischium, and *D*, a patient wearing the convalescent brace used for all pelvic foci.

ilium just above the sciatic notch was brittle. Only a few cubic centimeters of pus was encountered in the joint. The patient's recovery was uneventful. Four months later the sinus was again explored, and a small sequestrum was removed. Healing occurred in about one year. No bacterial organisms were recovered at operation. The diagnosis on the basis of the pathologic picture was chronic pyogenic osteomyelitis, with calcification of the joint surfaces.

CASE 4.—William S., white, aged 38, was admitted on Feb. 14, 1933, with symptoms of two and one-half years' duration. He had definite tenderness over the left sacro-iliac joint and a sinus just above the middle crest of the ilium. In January 1931 he was operated on by the Smith-Petersen method. The operative wound healed in four months after a stormy convalescence, but the original sinus never healed, nor was the patient relieved of his sciatica. A diagnosis of pyogenic osteomyelitis was made.

Operation.—Partial resection was done. The spines of the ilium were roughened and almost fused to the sacrum. The entire joint was destroyed, and the ilium was sclerotic and very thick. The sacral portion was necrotic at the level of the third segment, and the sacral canal was opened in eradicating this area. Blunt dissection of the soft parts of the pelvis led to an abscess. Several branches of the superior gluteal vein were accidentally torn but fortunately could be clamped and ligated. A moderate degree of shock followed. Staph. aureus and streptococci were recovered. The diagnosis on the basis of the pathologic picture was pyogenic osteomyelitis, with secondary productive changes in the joint. The postoperative convalescence was uneventful except for some intrapelvic hemorrhage. Several small transfusions of blood were given, followed by marked improvement in the general condition, and healing was sound in about six months.

CASE 5.—Earnest B., aged 48, was admitted to the hospital in June 1933, with symptoms of four months' duration. The insidious onset was described as a "bellyache." An abscess soon appeared posteriorly. The patient lost some weight and could not bear weight because of pain in the right hip. Fourteen small sequestrums extruded spontaneously. There was a slight scoliosis to the left and a small sinus over the right sacro-iliac region. The skin about this was dull red and edematous. Infiltration and marked tenderness were elicited in this region. A roentgenogram showed an extensive destruction of the entire sacro-iliac joint. A diagnosis of pyogenic osteomyelitis was made.

Operation.—Total resection was done. The iliac flap was rapidly removed with the aid of a motor saw. There was brisk hemorrhage from the smaller vessels. The entire joint was necrotic, but no free pus was encountered. The diagnosis on the basis of the pathologic picture was pyogenic osteomyelitis, with no signs of specific inflammation. There was moderate shock, and the wound did not do so well as was expected. The drainage was profuse. The patient died at home about four months after operation, from an unknown cause.

CASE 6.—Francis H., white, aged 20, had "silent" involvement of the left sacro-iliac joint of about six years' duration. He had multiple foci, including acute spondylitis, all of which necessitated drainage. The sacro-iliac joint was explored as a possible source of continued occasional metastatic foci and was considered to be the initial primary focus. A diagnosis of pyogenic osteomyelitis was made.

Operation.—Partial resection of the sacro-iliac joint was done in September 1933. The joint was found to be fused and obliterated for the most part. The posterior portion of the sacrum was friable. The ilium was dense and sclerotic. The pathologic process consisted of mild subacute nonspecific inflammatory changes. Healing occurred promptly.

CASE 7.—Charles G., white, aged 17 years, had symptoms of one year's duration. There was chronic involvement of the lumbosacral and both sacro-iliac joints. The patient was a very poor operative risk as he was emaciated and covered with decubiti. Operation was performed as a last resort. A diagnosis of pyogenic osteomyelitis was made.

Operation.—Bilateral partial resection was done in February 1934. No frank pus was encountered, but considerable necrosis was present. Staphylococci were recovered. The patient died in about three months.

According to the autopsy report the diagnosis was subacute osteomyelitis of the lumbosacral portion of the spine, the sacro-iliac joints and the innominate bones and thrombosis of the right common iliac and left iliac veins.

CASE 8.—Wayne M., white, aged 23, had metastatic involvement of the lumbosacral and both sacro-iliac joints of about eighteen months' duration. He was

very septic and ill. Retroperitoneal drainage was established through Petit's triangle, but he grew progressively worse. A diagnosis of pyogenic osteomyelitis was made.

Operation.—Partial resection of the sacro-iliac joint and evacuation of the retroperitoneal abscess were done in August 1932. The patient died one month later, after a stormy period.

According to the autopsy report the diagnosis was chronic suppurative arthritis of both sacro-iliac joints, osteomyelitis of the lumbosacral portion of the spine, abscess of the right psoas muscle, suppurative phlebitis of the left femoral vein, multiple metastatic abscess of the soft tissue, chronic osteomyelitis of the scapula, amyloidosis of the liver and spleen and septicemia.

Osteomyelitis of the Ilium.—CASE 9.—Margaret F., white, aged 12 years, was admitted to the hospital in 1934 with symptoms of three years' duration. After a local injury she complained of intermittent pain and aching in the left hip and the region of the thigh. She had occasional night cries. She soon became acutely ill and feverish and had severe pain in the left hip and the region of the thigh. Incision and drainage of the thigh were soon followed by spontaneous drainage. The patient was a total invalid after the onset of the symptoms. Examination revealed a sinus in the upper anterior one third of the left thigh. Acute pain was elicited in this region on digital pressure. The hip was fixed in flexion and adduction of 75 degrees, associated with flexion contracture of the left knee of 75 degrees. The general condition was fair. The sedimentation rate was not rapid. The white cell count was 21,300, and the red cell count was 3,400,000. The roentgenogram showed destruction of the entire wing of the left ilium. A diagnosis of pyogenic osteomyelitis was made (fig. 3 C and D).

Operation.—Total resection was done in March 1934. The approach was difficult because of the contracture of the hip. The sinus led to the true pelvis just over the ascending ramus of the pubis, and pus was encountered when this depth was reached. Three major areas of destruction were found in the ilium (fig. 4). All the periosteal and soft structures were dense and adherent. After complete débridement a fairly dry field remained. Staphylococci were recovered, and the pathologic picture was that of pyogenic osteomyelitis. The most extensive change histologically was an irregular reactive osteosclerotic inflammatory process. The bone marrow consisted of hyperemic fibrous tissue which still showed some cellular infiltration. Destructive activity was only moderate, even in the region of the crater abscess, which was covered by scar, on the surface of which the granulations were necrotic. Numerous purulent foci were still present in the more superficial marrow spaces and in the neighborhood of the periosteal abscess, which contained necrotic spicules and was otherwise in an advanced stage of organization. A diagnosis of chronic osteomyelitis with extensive osteosclerosis surrounding periosteal abscess formation was made. The patient had a rather stormy convalescence, but healing occurred in about one year, with little or no regeneration of the iliac wing.

CASE 10.—Gertrude G., white, aged 13 years, was admitted to the hospital in August 1933, with symptoms of two months' duration. The onset and course were subacute. The patient was fairly well nourished and walked with a limp on the left side. The left buttock was flat, and the left trochanter was less prominent than the right. A tender mass was palpated above the left hip joint, which exhibited limitation on rotation. The roentgenogram showed a destructive lesion of the iliac wing simulating tumor formation (fig. 3 A and B). A diagnosis of tumor or pyogenic osteomyelitis was made.

Operation.—Partial resection was done in August 1933. A tremendous amount of odorless edema and necrosis of the soft parts was encountered. The entire anterior two thirds of the upper half of the ilium was gone except for a small outer shell, which was sequestered. Within the iliac fossa were found many spiculed sequestrums the size of tooth picks in a mass of débris. The pathologic picture was that of subacute and chronic fibrous osteomyelitis. Histologic examination showed a great amount of young cancellous bone with irregular texture. The bony trabeculae were composed of lamellar bone, fibrous bone and even calcified cartilage in the central portion. In part there was an osteoid layer with signs of inflammation. Between the bony trabeculae in several areas larger masses of hyaline cartilage were interposed, and there was continuous transformation of cartilaginous tissue toward fibrous bone tissue, as is commonly the rule in

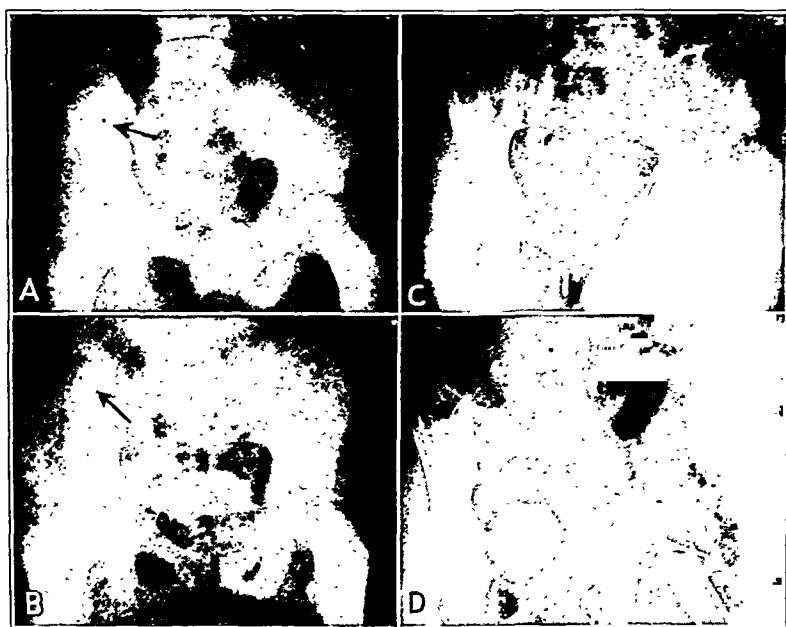


Fig. 3.—Preoperative and postoperative roentgenograms of the pelvis in two cases of iliac osteomyelitis. *A* (case 10) shows an untreated lesion of over two months' duration, which suggests tumor formation rather than inflammation. *B* was made after partial resection. *C* (case 9) shows an untreated lesion of almost four years' duration. *D* was made after total resection. A subtrochanteric fracture was noted after manual correction of the flexion deformity of the hip, performed at the time of operation.

callous formation or in myositis ossificans. The surrounding soft tissues were represented by transverse striated musculature, which showed the highest degree of edematous infiltration. Among the exudate cells, lymphocytes and polymorphonuclear leukocytes were present. A diagnosis was made of nonsuppurative subacute osteomyelitis and productive periostitis with marked inflammatory edema of the surrounding musculature. There was no suggestion of tumor formation.

The patient fully recovered in four and one-half months.

CASE 11.—Edna H., aged 11 years, was admitted to the hospital on May 13, 1935, with symptoms of ten days' duration. The onset was acute with pain in the right hip and groin associated with high fever, chills and vomiting. The child appeared to be acutely ill. The right hip was held in flexion. Considerable motion of the joint could be elicited, however, when her attention was distracted. The tenderness over the right groin was indefinite. In the right iliac fossa along the iliac crest backward definite tenderness and some muscle spasm were noted. The white cell count was 16,900, and the blood culture yielded staphylococci. In about five days a definite mass formed in the right iliac fossa, simulating an appendical abscess, and the temperature dropped to about 101 F. Serial roentgenograms revealed a supracotyloid destructive process (fig. 5). The diagnosis was pyogenic osteomyelitis as differentiated from acute appendicitis.

Operation.—Partial resection was done. A vertical incision from the iliac crest to the greater trochanter followed by blunt dissection exposed the supracotyloid region. The soft tissues were all edematous, and the outer cortex of the bone was soft and friable. No pus was encountered until the inner table was opened. Staphylococci were recovered, and the pathologic picture was that of acute pyogenic

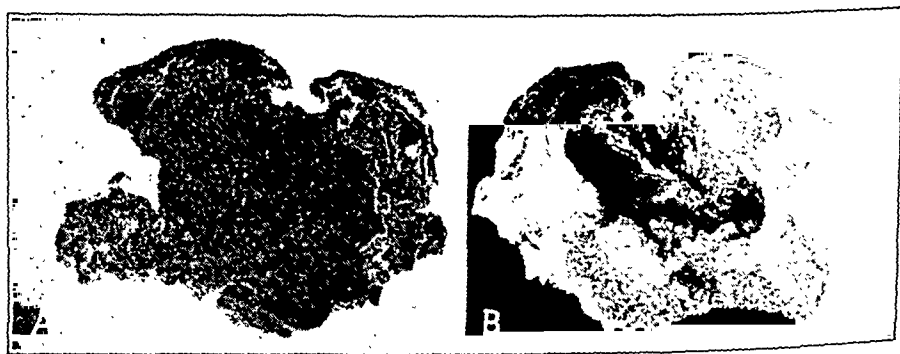


Fig. 4 (case 9).—Pathologic specimens of the iliac wing. *A*, the outer surface. The outer cortex was broken through in two places, one below the anterior superior spine and the second in the middle of the crest, and involved the cartilaginous apophysis as well as the bone. The bone was rather smooth and in many places was covered by densely adherent granulation tissue. The outer cortex formed a shell-like thin layer, whereas the inner cortex, so far as it was preserved, showed considerable thickening. *B*, the inner surface, showing a typical crater defect, with lateral displacement of the outer cortex.

osteomyelitis. The patient continued to have a low grade fever, which subsided only after counterincision and drainage along the iliac crest were performed. Healing occurred in about four months, with a residual ankylosis of the hip joint in good position.

CASE 12.—John S., white, aged 41, was admitted to the hospital on Feb. 21, 1936, with symptoms of forty-one years' duration. The present flare-up followed a pathologic fracture of the right humerus. Local symptoms came on acutely with sharp pain about the right hip and flank, and a perirectal abscess presented soon afterward. This was incised and drained. The roentgenograms showed extensive honeycombing and destruction of the iliac wing, hip and trochanteric region (fig. 6). A diagnosis of pyogenic osteomyelitis was made.

Operation.—Partial resection was done on March 31. Numerous sequestrums were encountered. The main pathologic process in the ilium centered about the anterior third of the wing of the ilium. There was a typical crater-like destruction on the pelvic surface, with a considerable collection of débris and pus. A sinus had apparently burrowed downward into the true pelvis. The ilium was tremendously thickened. The hip joint itself was entirely denuded of cartilage and destroyed, but allowed manual correction. There was a moderate degree of post-operative shock. Four days later sepsis developed. The wound, which for one reason or another had been partially closed and inadequately drained, was opened and found filled with purulent exudate. The patient did not rally and died on April 12 of peritonitis, incident to a secondary infection with colon bacilli from the perianal fistula. This was the only case in which the Orr technic was not observed.



Fig. 5 (case 11).—*A*, roentgenogram of the pelvis, illustrating a prepuberty supracotyloid lesion twelve days after the onset of symptoms, which already involved the superior rim of the acetabulum. (The patient was referred by Dr. H. S. Conrad.) *B*, a roentgenogram taken two months later. The disease had extended to the wing of the ilium and some wandering of the acetabulum and head of the femur had occurred.

CASE 13.—Gloria M., aged 11 years, was admitted to the hospital on April 24, 1936, with symptoms of three days' duration. She fell while roller skating and struck the left hip. That night she had a slight chill and fever, accompanied by anorexia and marked constipation. The fever and pain in the left hip persisted. On examination she was found to be mildly septic. The left hip was held in flexion and adduction, but was quite freely movable. There were marked tenderness over the lateral portion of the ilium and pubis and some tenderness in the left iliac

fossa. The patient was placed in traction, and general measures were instituted. The white cell count was 6,000, and the sedimentation rate was rapid. The fever was sustained. On the fifth day definite infiltration appeared below the anterior crest of the ilium. The roentgenogram was still normal (fig. 7 *A*). The general condition was improved. A diagnosis of pyogenic osteomyelitis was made.

Operation.—On April 29 an external subperiosteal abscess was drained just below the anterior crest of the ilium. The bone was very hemorrhagic but appeared slightly pale at the anterior metaphysial border. A fragment was removed for examination. The pathologic report was acute osteomyelitis, and staphylococci were recovered. A subacute course followed, and in about two weeks roentgenographic delineation of the lesion was noted (fig. 7 *B*), and partial resection (May 11) of the ilium was performed. The supracotyloid region was

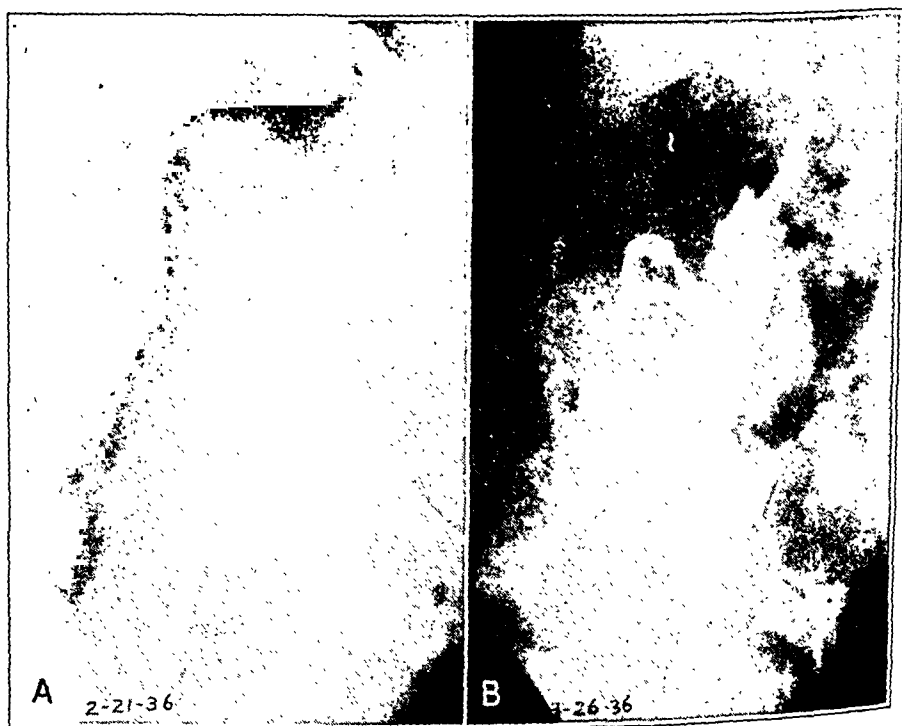


Fig. 6 (case 12).—Roentgenograms showing an iliac lesion involving the hip joint and femur of forty-one years' duration with a recent flare-up. The injection of iodized poppy-seed oil 40 per cent into the perirectal sinus revealed the extensiveness of the soft tissue abscess and the dangers of secondary infection from the rectum, especially after radical operation. (The patient was referred by Dr. Paul Forgrave.)

not involved, and an iliac abscess was now encountered and drained. Complete recovery followed subsequent treatment of a "silent" tibial metastatic lesion. Healing occurred in about five months.

Osteomyelitis of the Ischium.—CASE 14.—Russel C., aged 16 years, was admitted to the hospital on Nov. 2, 1933, with symptoms of eight weeks' duration. The onset began suddenly, with pain in the left hip, limpness and fever. This was aggravated by sitting and jarring. The patient had a series of boils three weeks previously. He had lost 27 pounds (12.2 Kg.) in weight. The leukocyte count



Fig. 7 (case 13).—*A*, roentgenogram of the pelvis five days after the onset of symptoms. No abnormal changes are demonstrated. *B*, a roentgenogram made twenty-one days after the onset. Destructive and productive changes appear at the lateral margins of the left ilium.



Fig. 8 (case 13).—Roentgenograms of the resected portion of the ilium twenty-two days after the onset of symptoms. The destructive process about the secondary epiphysal centers is evident, although the child was only 11 years of age. The arrow points to the anterior superior spine. (Presented by courtesy of Dr. A. B. McGlothlan.)

was 14,000. There were occasional radiating pain in the left knee, and the hip and knee had drawn up. Examination revealed a well developed but moderately emaciated boy. The left lower extremity was held in 90 degrees of external rotation and 50 degrees of flexion. He held the left hip guardedly. The inguinal glands were enlarged, and there were no local signs of inflammation but some induration about the left ischiorectal fossa and definite tenderness over the left ischial tuberosity. Rectal examination revealed tenderness of the left ischium. The white cell count was 10,000. The roentgenograms showed a marked honeycombing and destructive process in the left ischium (fig. 9 *C* and *D*). A diagnosis of tumor or pyogenic osteomyelitis was made.

Operation.—Total resection was done in November 1933. There was no frank pus, but considerable necrosis and marked parosteal edema were present. There



Fig. 9 (case 14).—Serial roentgenograms of the pelvis. In *A*, taken several days after the onset of symptoms, no ischiac pathologic process was noted. In *B*, taken about eight weeks after the onset of symptoms, the pathologic changes in the ischium simulated tumor rather than an inflammatory lesion. *C* was taken immediately after resection of the ischium and *D* about four months later, when regeneration was taking place.

was no periosteal proliferation. The bone was hemorrhagic and shaggy and strongly suggested tumor formation. *Staphylococcus aureus* was recovered from the necrotic bone, and osteomyelitis was diagnosed pathologically. Histologic examination showed necrotic marrow and some cortical sequestration, but the cartilaginous portion of the ischium was well preserved. In spite of the predominance of bone absorption, production of new bone was nevertheless occurring. In some places the marrow was densely infiltrated by polymorphonuclear leuko-

cytes. The granulations rapidly changed into dense fibrous tissue, with almost immediate hyaline degeneration. While no frank pus was visible, there was nothing to indicate tumor formation.

The convalescence was uneventful. The wound healed in four months. The external rotation deformity of the hip present on admission awaits corrective osteotomy.

CASE 15.—Hazel M., white, aged 6 years, was admitted to the hospital on Feb. 4, 1934, with symptoms of two days' duration. She began to limp suddenly two days before her admission to the hospital. She became ill rapidly and had a high fever, the temperature reaching 106 F. Several days before the onset she had an infected blister on the foot. On admission she was flushed and almost moribund. The hip was held in flexion but could be moved substantially. Pressure over the ischium on rectal examination caused the patient to wince even though she was practically unconscious. Aspiration in the region of the ischium with the patient under anesthesia gave negative results. (A tentative diagnosis of pyogenic osteomyelitis was made at this time.) The course was stormy, and several pyemic abscesses and also metastasis of the right fibula developed. In about six weeks the ischiatic lesion was definitely noted in serial roentgenograms (fig. 10), and the vulva was swollen.

Operation.—Total resection and removal of the floor of the acetabulum were done. On exploration medially and up toward the pubis, several cubic centimeters of frank pus were exuding from this region. The entire ischium was roughened. This reaction impressed one as being of a collateral nature. That portion of the ischium uniting with the descending portion of the pubis lifted out easily but did not appear to be definitely sequestered. The floor of the acetabulum was, however, necrotic. Moderate shock ensued. Staphylococci were recovered, and the pathologic picture was that of pyogenic osteomyelitis. The changes in the infra-acetabular portions of the bone revealed changes chiefly of a collateral ischemic nature. The fibrous bone showed active bone formation leading to osteosclerosis. The cortical bone was alive, whereas the spongy bone showed necrosis. The acetabular region, the initial and primary seat of involvement, showed entire areas where the old spongy bone had disappeared and were occupied by dense fibrous bone, in greatest part osteoid. The small remnants of fatty bone marrow still showed inflammatory cellular infiltration. A diagnosis of subacute and chronic nonsuppurative osteomyelitis was made (osteomyelitis following invagination of old necrotic spongy bone by new bone apposition). The convalescence was uneventful, and the wound healed in three months with regeneration of the ischium (fig. 2 C).

CASE 16.—Wanda S., aged 13 years, had symptoms of three months' duration, which were of subacute onset and course. On admission of the patient to the hospital it was difficult to localize the trouble accurately. In March 1933 the left hip was drained through a lateral incision, and no definite pathologic process was noted. In August 1933 the upper anterior portion of the ilium was exposed, and only sclerotic bone was encountered. The clinical course continued to show the presence of an active focus, which was finally located in the left ischium, after the vulva became edematous.

Operation.—Total resection was done in November 1933. Through the usual approach the entire ischium was found to be necrotic and in a bed of pus. Staphylococci were recovered, and the pathologic diagnosis was chronic productive periostitis, subacute osteomyelitis and arthritis. The convalescence was uneventful, and the wound healed in three months, at which time the ischium had regenerated

CASE 17.—Jule L., aged 16 years, was admitted to the hospital on July 22, 1935, with symptoms of eighteen days' duration. The onset was subacute and followed an indirect injury to the left hip. There was fever but no chills, and the pain was referred to the left hip and occasionally to the left knee medially. The patient appeared to be acutely ill. The left hip was held in flexion and some external rotation. Gentle manipulation elicited a fair range of motion, however. The entire left buttock was tense and tender and warm. Rectal examination

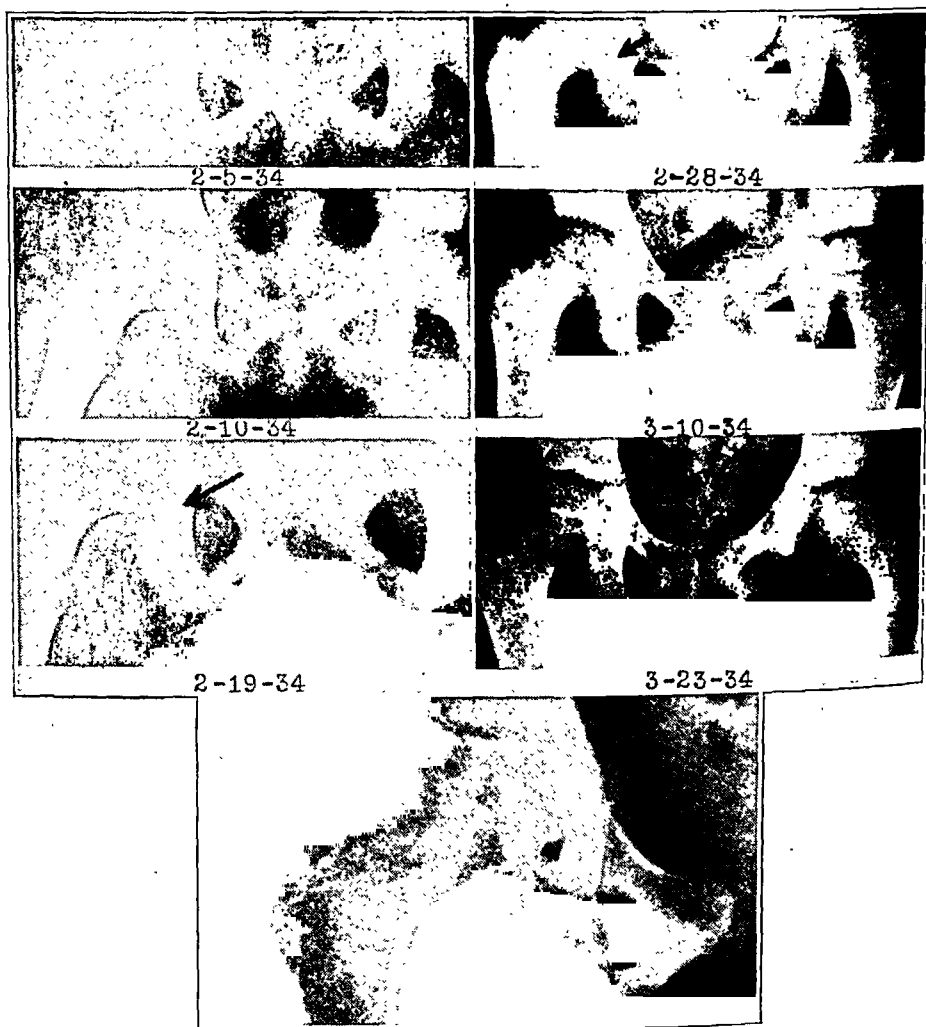


Fig. 10 (case 15).—Serial roentgenograms of the pelvis in a child, beginning three days after the onset of symptoms. Slight infra-acetabular changes were noted fourteen days later (2/19/34), but convincing evidence of destruction did not appear until thirty-six days after the onset of symptoms (3/10/34). The next picture was made after resection of the ischium and the last picture reveals regeneration about four months after operation.

revealed maximum tenderness over the ischium. The white cell count was 27,000, and the blood culture was negative. The roentgenogram is shown in figure 11. A diagnosis of pyogenic osteomyelitis was made.

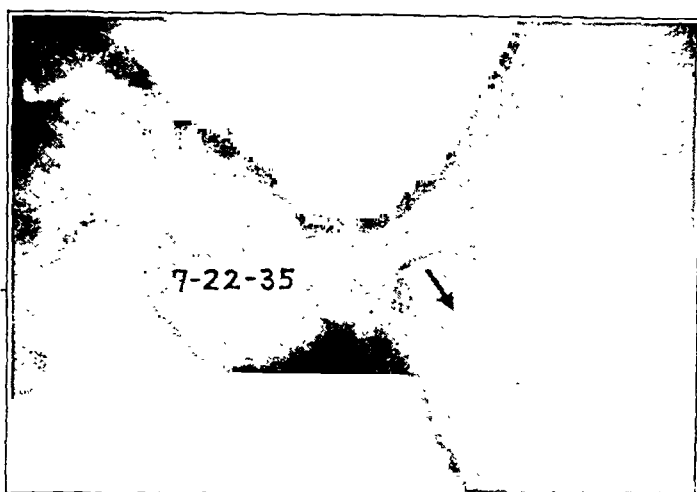


Fig. 11 (case 17).—Roentgenogram of the pelvis taken eighteen days after the onset of symptoms. The shadow of the soft tissue abscess predominates and obscures the skeletal ischiac changes. (The patient was referred by Dr. H. S. Forgave.)

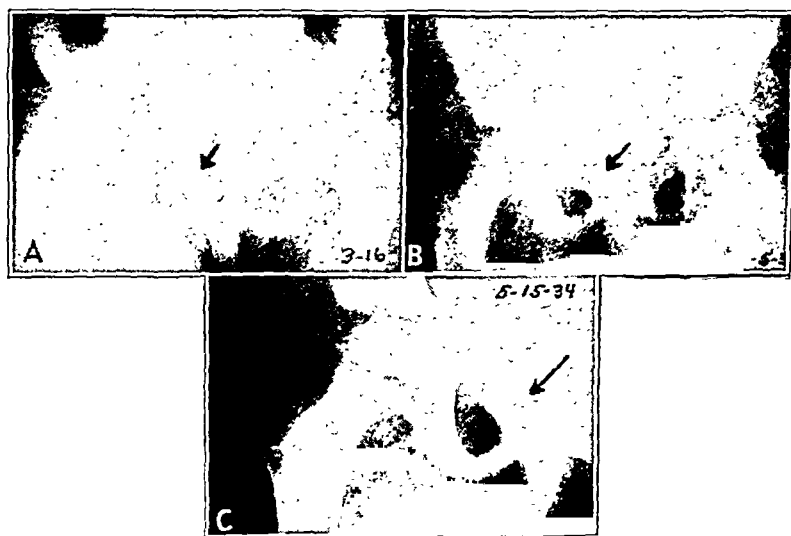


Fig. 12. (case 18).—*A*, roentgenogram showing a juxta-epiphyseal pubic lesion three weeks after the onset of symptoms. The abscess and flexion of the hip blur the skeletal outlines. *B*, roentgenogram taken three weeks after operation. *C*, roentgenogram taken about six weeks later. There had been no extension, and the curetted bone is clear in outline.

Operation.—Total resection was done. A huge subgluteal collection of pus which involved the subgluteal bursa was evacuated. The ischium was bare owing to the stripping action of the pus. Most of the destruction was at the tuberosity, but the entire bone was removed because of the extensive purulent dissection already present. Staphylococci and streptococci were recovered. The pathologic diagnosis was subacute and acute pyogenic osteomyelitis. In spite of the radical resection, the patient's course continued to be of the low grade septic type, until the floor of the acetabulum was removed for more adequate drainage. The convalescence was then good, and healing occurred in about six months. There was residual ankylosis of the hip in good position.

Osteomyelitis of the Pubis.—CASE 18.—Phyllis S., aged 5 years, was admitted to the hospital on March 16, 1934, with symptoms of three weeks' duration. The condition was of sudden onset, with severe pain in the right groin associated with fever. She remained in bed with the right hip drawn up. She lost from 10 to 15 pounds (4.5 to 6.8 Kg.) in three weeks and appeared to be acutely ill and septic. The temperature was 104 F. There were marked tenderness over the inguinal ligament and some swelling of the right mons pubis and also the vulva of a lesser degree. The right hip was acutely flexed, but otherwise was normal. When the patient's attention was diverted, the hip could be moved. The white cell count was 32,000. The rectal examination (under anesthesia) revealed definite infiltration in the pubic region, the descending ramus and the medial wall of the right side of the pelvis. When the thigh was extended a fluctuating mass appeared in the right groin. The diagnosis made was pyogenic osteomyelitis as differentiated from appendical abscess.

Operation.—Drainage and curettage were done in March 1934. Through a curved incision about $3\frac{1}{2}$ inches (8.9 cm.) long, cutting obliquely across the medial half of Poupart's ligament, an abscess cavity was entered just above Poupart's ligament and about 50 cc. of an odorless brownish creamy pus was found. Digital exploration showed this to be a granulation-lined subcutaneous abscess. About 100 cc. of thick green pus kept welling up from below Poupart's ligament, and this was found to be coming from Scarpa's triangle. Further digital examination of the right pubis showed a small localized necrotic area at the chondro-osseous border portion of the body of the pubis. This was carefully curetted out. Staph. aureus was recovered. The pathologic picture was that of acute osteomyelitis. Healing occurred in six weeks after an uneventful convalescence.

CIRCULATORY DISTURBANCES REFLEXLY INAUGURATED BY STIMULATION OF THE CELIAC PLEXUS

A PRELIMINARY REPORT

CHARLES L. BURSTEIN, M.D.

AND

E. A. ROVENSTINE, M.D.

NEW YORK

Circulatory disturbances coincident with surgical manipulations in the upper part of the abdomen have frequently been described. A transitory initial rise in the blood pressure succeeded by a fall as a rule follows manipulation of the abdominal viscera. Recently, in a case in which a difficult cholecystectomy was performed, at the stage when operative manipulation was maximum, an unusual phenomenon was observed in the course of routine sphygmomanometry by the auscultation method. The blood pressure, which had remained constantly within normal limits with a difference of 60 mm. of mercury between the systolic and the diastolic level, suddenly became unobtainable for twenty minutes, although the peripheral pulse could still be palpated and was not materially altered in rate. At first, the mercury column being allowed to fall very slowly, a single beat was heard at about the level of the previous systolic pressure. Within a few minutes this single beat could not be obtained. It was further noted that when the operative manipulations had ceased, the normal auscultation sounds were again obtained and at a level comparable to the previous determinations. Thereafter, careful and frequent determinations on the blood pressure were made during all operations on the upper part of the abdomen. The phenomenon described was soon obtained in the course of another cholecystectomy and during gastric resection. The patients had been given morphine and atropine preoperatively. In an attempt to account for the circulatory disturbance noted, observations were made in the laboratory to determine the effects on the blood pressure curve obtained during intra-abdominal manipulations.

EXPERIMENTAL STUDY

Dogs were used for the experiments, and attempts were made to reproduce the same operative conditions. Preoperative medication consisted of 5 mg. of morphine sulfate and 0.1 mg. of atropine sulfate per kilogram of body weight

From the Department of Anesthesia, Division of Surgery and the Laboratory of Experimental Surgery of New York University College of Medicine.

administered subcutaneously one hour before anesthesia. Ether anesthesia was then induced by the open cone method, and an endotracheal tube was passed through the mouth into the trachea and made air tight by inflating a cuff surrounding it. This tube was connected to a rebreathing bag, and a canister containing soda lime was inserted between the two so that the technic of carbon dioxide absorption¹ could be maintained. Ether and oxygen were supplied to the system by means of a Foregger metric machine. The blood pressure was recorded from a cannula inserted into the femoral artery and connected to a mercury manometer which registered on a kymograph. Respirations were recorded at the same time by means of a pneumograph applied about the thoracic region.

The peritoneum was opened by a long midline incision. Traction on the various viscera and intra-abdominal exploration resulted in circulatory disturbances consisting of a small rise in the mean arterial blood pressure and a slight reduction in the pulse pressure. Traction on the gallbladder, as shown by Brewer and Luckhardt,² was followed by apnea (chart 1 *B*), and a slight rise in the blood pressure was recorded. Exploration in the region of the solar plexus and

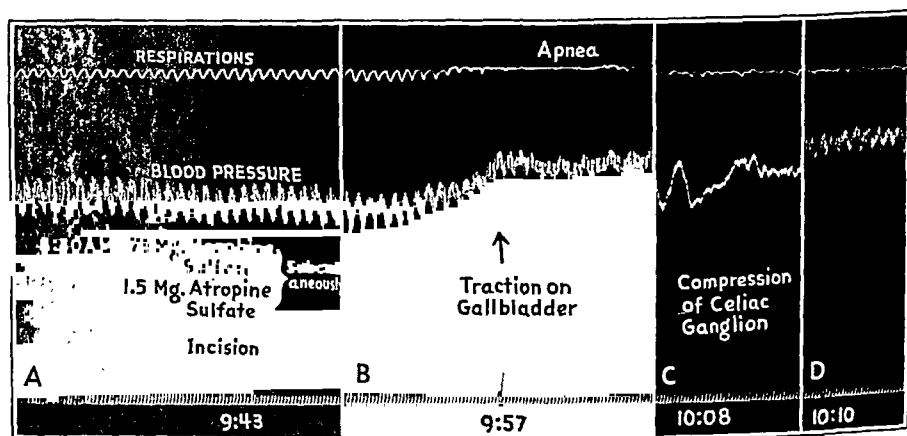


Chart 1.—Serial sections from an experiment on dog 34, which weighed 15 Kg. At 8:30 a. m. 75 mg. of morphine sulfate and 1.5 mg. of atropine sulfate were administered subcutaneously. At 9:43 a. m., when the initial incision was made, the blood pressure was normal, as indicated in *A*. In *B* are shown the effects of traction on the gallbladder at 9:57 a. m., which included apnea, a rise in the mean blood pressure and a reduction in the pulse pressure. Compression of the celiac ganglion at 10:08 a. m. brought about a marked reduction in the pulse pressure and no appreciable change in the mean blood pressure, as shown in *C*. After the compression of the celiac ganglion was released at 10:10 a. m., the pulse pressure recovered, as shown in *D*.

especially compression of the celiac ganglion gave an immediate response characterized by a marked reduction in the pulse pressure without a fall in the mean blood pressure (chart 1 *C*). The diminution of the range between the systolic

1. Waters, R. M.: Utility of Carbon Dioxide Absorption from Anesthetic Mixtures, *Anesth. & Analg.* 3:20 (Feb.) 1924.

2. Brewer, N.; Luckhardt, A. B.; Lees, W. M., and Bryant, D. S.: Reflex Closure of the Glottis by Stimulation of Afferent (Visceral) Nerves, *Anesth. & Analg.* 13:257, 1934.

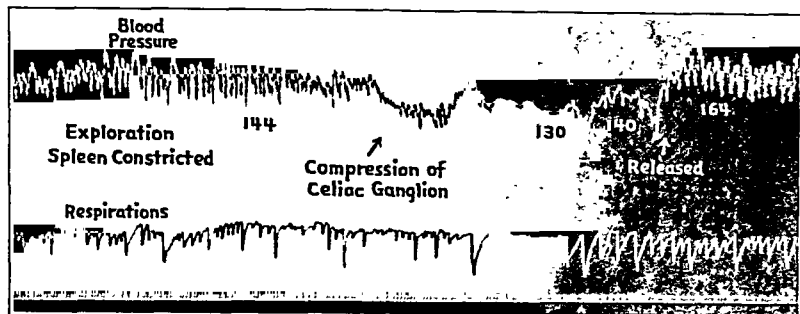


Chart 2.—A tracing showing the reflex in its entirety. Atropine sulfate was given previously.

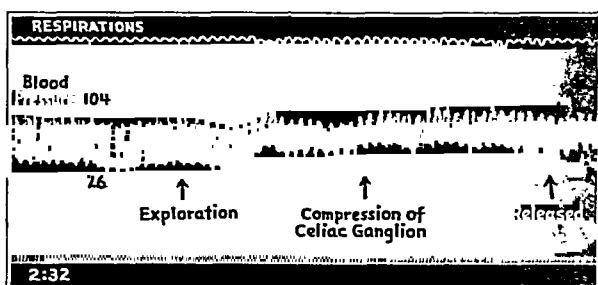


Chart 3.—A tracing showing the reflex when atropine sulfate was not administered.

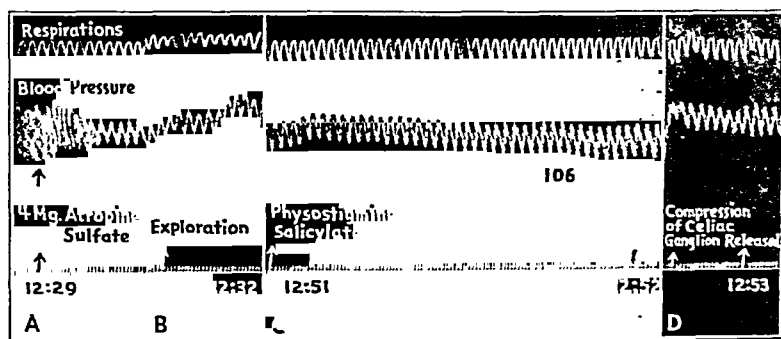


Chart 4.—Serial sections from an experiment on dog 201, which weighed 22 Kg. One hundred milligrams of morphine sulfate was administered at 10:30 a. m. In *A* is shown the immediate reduction of the pulse pressure after the intravenous injection of 4 mg. of atropine sulfate at 12:29 p. m. Intra-abdominal exploration at 12:32 p. m., indicated in *B*, was followed by compression of the celiac ganglion. The intra-abdominal exploration caused a reduction in the pulse pressure and a rise in the mean blood pressure, while compression of the celiac ganglion caused further and more marked reduction in the pulse pressure and no change in the mean blood pressure. After twenty minutes with no improvement in the pulse pressure, an intravenous injection of physostigmine salicylate at 12:51 p. m. readily caused a return of the pulse pressure, as shown in *C*. Intra-abdominal exploration was followed by compression of the celiac ganglion after the administration of physostigmine salicylate at 12:53 p. m., as indicated in *D*. The first procedure caused only a slight reduction in the pulse pressure and a slight rise in the mean blood pressure. The latter procedure caused a very slight further reduction in the pulse pressure and no change in the mean blood pressure.

and the diastolic pressure became so marked that the pulse pressure practically disappeared. At the same time the abdominal muscles became more tense, and the intestines protruded from the wound. On releasing the compression the pulse pressure returned (chart 1 *D*). Similar tracings were secured following the application and release of pressure on the celiac ganglion (chart 2). This reaction was repeated in several dogs prepared and experimented on in the same manner.

It was further noted that when atropine sulfate was not administered the production of this reflex was either absent or greatly diminished, the pulse pressure falling but slightly (chart 3). However, if a dog which had not received atropine sulfate and did not show this reflex was given an intravenous injection of the drug a definite reduction in the pulse pressure (chart 4 *A*) would immediately result, and compression of the celiac ganglion would then be followed by a further reduction in the pulse pressure (chart 4 *B*), which would be maintained for a long time. Furthermore, if physostigmine salicylate was given intravenously the pulse pressure was markedly increased (chart 4 *C*). After physostigmine salicylate was administered, efforts to elicit this celiac plexus reflex would result in only a slight reduction of the pulse pressure (chart 4 *D*).

It was therefore evident that compression of the celiac ganglion caused a reflex reduction in the pulse pressure and that paralyzing the vagus nerves with atropine sulfate intensified the reflex, whereas stimulation of these nerves with physostigmine salicylate prevented entirely or reduced an already existing reflex. It is interesting to note that Capps and Lewis,³ in their work on pleural reflexes, have found that stimulation of the pulmonary vagus nerves (instead of their paralysis) is followed by a "cardio-inhibitory reflex, in which the heart is slowed and the pulse tracings make violent excursions, with a great range between systolic and diastolic pressure."

Further experimental studies to show the mechanism of this reflex are in progress and will be reported at a later date.

SUMMARY

Stimulation of the celiac plexus when atropine sulfate has been previously administered produces a marked reduction in the pulse pressure with maintenance of the mean arterial blood pressure.

Stimulation of the celiac plexus when atropine has not been administered previously causes little or no change in the pulse pressure.

Manipulations in the upper abdominal cavity cause a reduction in the pulse pressure, especially when atropine sulfate has been given previously.

Administration of physostigmine salicylate reduces the reflex.

477 First Avenue.

3. Capps, J. A., and Lewis, D. D.: Pleural Reflexes, Surg., Gynec. & Obst. 7:243, 1908.

SIXTY-THIRD REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

JOHN G. KUHN, M.D.

EDWIN F. CAVE, M.D.

SUMNER M. ROBERTS, M.D.

JOSEPH S. BARR, M.D.

AND

ROBERT J. JOPLIN, M.D.

BOSTON

JOSEPH A. FREIBERG, M.D.

CINCINNATI

JOSEPH E. MILGRAM, M.D.

NEW YORK

AND

ROBERT I. STIRLING, F.R.C.S. (Edin.)

EDINBURGH, SCOTLAND

CONGENITAL DEFORMITIES

Congenital Dislocation of the Hip.—Van Gorder¹ reviews the end-results in 58 cases of dislocation of the hip (73 hips) in which treatment was given at the Massachusetts General Hospital during the period from 1923 to 1933. Sixteen of the hips were treated by closed reduction. The results in 10, or 62 per cent, were rated as excellent; i. e., there were a negative Trendelenburg sign, normal motion and no limp, shortening or atrophy. The results in 4, or 25 per cent, were rated as good; i. e., there were a slight limp, a positive Trendelenburg sign, excellent function and no disability. The results in 2, or 12.5 per cent, were rated as fair. Fifteen hips were treated by open reduction. The results in 1 were rated as excellent and in 3 as poor. Bony ankylosis occurred in 2, and a stripping of all structures from the neck and trochanters was done on the last 2 hips preliminary to heavy traction and open reduction. The 8 hips treated by open reductions plus a shelf operation showed no excellent results; the results in 2 were rated as good, in 1 as "fair" and in 2 as poor, and bony ankylosis occurred in 3. Sixteen hips treated by

This report of progress is obtained from a review of 144 papers selected from 296 titles relating to orthopedic surgery and appearing in the medical literature approximately between Nov. 1, 1936, and March 1, 1937. Only those which indicated progress were selected for review.

1. Van Gorder, G. W.: New England J. Med. **215**:613 (Oct. 1) 1936.

a shelf operation alone showed no excellent results; the results in 8, or 50 per cent, were rated as good, in 4, or 25 per cent, as fair and in 4 as poor.

Summarizing these statistics in a different way: Good functional results were obtained in 88 per cent of the hips treated by closed reduction, in 27 per cent of those treated by open reduction, in 25 per cent of those treated by open reduction plus a shelf operation and in 50 per cent of those treated by a shelf operation alone. While the author feels that these results are far from satisfactory, he points out that two thirds of the patients in this study were over 5 years of age when treated.

Congenital Hallux Valgus.—Hoffmann² reports 4 cases of congenital deviation of the second phalanx of the great toe and was able to find 4 similar cases described in the literature. The author considers the condition as a congenital arrest in development in the epiphysis of the phalanx. Correction was obtained by a wedge osteotomy of the proximal phalanx of the big toe.

Brittle Bones and Blue Scleras in 5 Generations.—Blue scleras, fragile bones, a tendency to deafness and marked relaxation of the ligaments constitute a clinical entity according to Hills and McLanahan.³ Data concerning 51 persons in 5 generations, all traced back to a common female ancestor, revealed that 27, or nearly half, were affected; 60 per cent were females. Deafness was manifest in 57 per cent. The blue sclera is generally attributed to thinness of the sclerotic coat, through which the choroid shines. The fractures are not likely to be present at birth but appear throughout childhood until puberty is reached. Union is prompt and complete. The etiology is unknown, but the fact that the fractures appear to cease at puberty would lead one to suppose that approach along endocrine lines offered greatest promise.

DISTURBANCE OF GROWTH

Tibia Vara.—Thirteen new cases and reports of 15 collected from the literature are reviewed by Blount⁴ to illustrate the occurrence of an osteochondritis similar to coxa plana and Madelung's deformity but located at the medial side of the proximal tibial epiphysis. The resulting abrupt angulation into varus with back knee and internal rotation of the leg is usually confused with rickets. The roentgenographic picture and the pathologic changes are like those of coxa plana and similar to those of chondrodysplasia but are quite different from those of rickets. The changes may appear in the first year or two of life (infantile type) as a

2. Hoffmann, H.: Ztschr. f. Orthop. **65**:353, 1936.

3. Hills, R. G., and McLanahan, S.: Brittle Bones and Blue Scleras in Five Generations, Arch. Int. Med. **59**:41 (Jan.) 1937.

4. Blount, W. P.: J. Bone & Joint Surg. **19**:1, 1937.

developmental exaggeration of the normal, with sloping epiphysis and beaklike, recurving metaphysis. Similar deformity may occur just before puberty (adolescent type), secondary probably to local trauma or possibly to infection. The age at which the deformity is observed is more important than the causative factor in determining the roentgenographic appearance. The roentgenographic picture presented by the infantile type gradually changes to that presented by the adolescent type, so that later the two can be distinguished only by the history. Treatment should be directed toward the mechanical relief of strain until the deformity is stationary or until the epiphysis is closed. Simple osteotomy is desirable in the correction of marked deformity. If it is done before the angulation becomes stationary, some degree of recurrence may be anticipated.

TUBERCULOSIS

Multiple Arthritis in Tuberculous Subjects.—Collins and Cameron⁵ sound a warning against the too early acceptance of a tuberculous etiology in cases of insidious arthritis occurring in presumably tuberculous patients, as this often results in prolonged and expensive immobilization, which is prejudicial to subsequent recovery of function. They suggest that in all such cases expectant treatment should be adopted. This should consist of maintenance of general hygiene and rest in bed without immobilization until unequivocal evidence of the tuberculous or non-tuberculous nature of the joint appears or is obtained by examination or by biopsy of material obtained by aspiration.

Glutathionemia in Tuberculosis of Bones.—Altschuler⁶ studied the glutathione content of the blood from children with tuberculosis of the bones and joints. The more severe the tuberculous lesion, the higher were the values for glutathione in the blood. The author feels that fluctuations in the glutathione content of the blood assisted in estimating the course of the disease. A review of the literature is given.

Result of Spinal Fusion in Tuberculous Spondylitis.—Grigorescu and Vasiliu⁷ report on 82 of 182 cases of tuberculous spondylitis in which an Albee fusion operation was performed. Postoperative fixation consisted of three months of rest in a plaster bed followed by the use of back supports. After six months the patients were permitted to return to their occupation. Twenty-four were well from seven to nine years after the operation; healing was taking place in 50 with considerable improvement from three to four years after the operation. In eight of those with abscesses, the abscesses had healed. In 2 there was no change and the abscesses persisted. One with paraplegia was somewhat

5. Collins, D. H., and Cameron, C.: *Brit. J. Surg.* **24**:272, 1936.

6. Altschuler, M. M.: *Acta tuberc. Scandinav.* **10**:370, 1936.

7. Grigorescu, I. I., and Vasiliu, A.: *Beitr. z. klin. Chir.* **164**:1, 1936.

improved. Four had died from three months to five years after the operation. One died of sepsis four days after the operation.

Use of Biopsy Specimens Obtained by a Punch in the Diagnosis of Tuberculosis of the Knee Joint.—In connection with the arthroscope, which resembles a cystoscope and is used for direct observation of the knee joint, Burman and his co-workers⁸ have developed a punch for obtaining biopsy specimens from the knee joint. It is inserted through the same puncture hole used for the arthroscope. The specimen is secured blindly, although the arthroscope is first used for localization. In 8 cases of proved tuberculosis of the knee, the diagnosis was made in 6 on the basis of specimens secured with this instrument. This method is offered as another diagnostic test for tuberculosis of the knee and is considered by the authors as preferable to the radical method of securing a biopsy specimen, as advocated by Hibbs.

OSTEOMYELITIS

Osteomyelitis of the Bones of the Hand.—Osteomyelitis of the bones of the hand secondary to infection of the soft tissue is often treated radically by guttering or by removal of the bone. Koch,⁹ whose experience is extensive, condemns such radical surgical methods. He states:

The essential factors in the treatment of osteomyelitis of the bones of the hand are adequate drainage of the overlying soft parts, cleanly surgical care, and avoidance of trauma—by irritating chemicals, by addition of infection from without, and, particularly, by the use of curette and chisel. If death of bone takes place a line of demarcation forms and the necrotic bone, if it is not extruded spontaneously, can be removed without trauma. To attempt to determine a line of demarcation by surgical intervention too frequently results in destruction of living bone and extension of infection, and often makes recovery of the affected bone impossible.

POLIOMYELITIS

Humoral Antibodies and Resistance to Poliomyelitis.—Sabin and Olitsky¹⁰ found that monkeys recovering from a paralytic attack of poliomyelitis acquired humoral antibodies slowly two months after the attack. Convalescent monkeys showed resistance to reinfection by the nasal route long before antibodies appeared in their serum. Vaccinated monkeys often remained susceptible to nasal infection when their serum neutralized the virus. Humoral antibodies do not seem to have the same significance in vaccinated monkeys as in monkeys recovering from an attack of poliomyelitis.

8. Burman, M.; Finkelstein, H., and Mayer, L.: *Am. Rev. Tuberc.* **34**:663, 1936.

9. Koch, S. L.: *Surg., Gynec. & Obst.* **64**:1, 1937.

10. Sabin, A. B., and Olitsky, P. K.: *J. Exper. Med.* **64**:739, 1936.

CHRONIC ARTHRITIS

Fibrositis.—Slocumb¹¹ states that “fibrositis” is the commonest form of acute or chronic “rheumatism.” The term appears in the foreign literature frequently but is seldom seen in the American literature. The author, nevertheless, believes that a condition exists which should be referred to as “fibrositis” rather than by any other term. Although in most cases the exact etiology is unknown, fibrositis is believed to be due to some unidentified infection or toxin. He believes that primary fibrositis should include (1) “myositis;” (2) “bursitis;” (3) periarticular fibrositis, or so-called “capsular rheumatism;” (4) tendinous fibrositis, which leads to Dupuytren’s contracture of the palm; (5) perineural fibrositis, of which “sciatica” and “brachial neuralgia” are the common types, and (6) panniculitis. In the first stage of the process there is a low grade inflammatory serofibrinous exudate with proliferating fibroblasts and newly formed blood vessels; in the second stage, indurated, tender thickened tissue or subcutaneous nodules may be produced which may show dense inflammatory hyperplasia of fibrous tissue, thickened blood vessels and inflamed nerve fibrils without leukocytic reaction; in the third stage, when the inflammatory stage has passed, indurations may disappear or remain as painless nodules or capsular thickening which may affect such regions as the shoulders or the palms. The author feels that the differential diagnosis between these two conditions lies in the abundant indirect evidence of the persistent integrity of the joint cavity in fibrositis; that is, the disease is at the joint and not within the joint. Laboratory findings revealed little or no change in the sedimentation rate in cases of periarticular fibrositis in contrast to the rapid rate in cases of atrophic arthritis. Likewise, roentgenographic findings are demonstrated only in cases of atrophic arthritis. Finally, the author feels that when objective changes, systemic manifestations and alterations of laboratory findings, known to be relatively consistent in cases of atrophic arthritis, remain persistently absent, the arthralgia, stiffness and articular thickening can be, with no little confidence, ascribed to periarticular fibrositis, and the fear of impending arthritis can be laid aside.

THE SHOULDER

Scaglietti¹² discusses obstetric lesions of the shoulder thoroughly and describes the method of therapy as used by Putti. The article is based on a study of 199 cases in which therapy was given at the Instituto Rizzoli from 1899 to July 1935. The condition was unilateral in 93 per cent of the cases and bilateral in 6.5 per cent. In 62 per cent of the total number the right shoulder was involved. Conservative treat-

11. Slocumb, C. H.: J. Lab. & Clin. Med. 22:56, 1936.

12. Scaglietti, O.: Chir. d. org. di movimento 22:183, 1936.

ment was used in 75 per cent of the cases and surgical treatment in 25 per cent. The cases were divided into three groups: those of obstetric trauma of the joint or the superior humeral epiphysis or distortion of the joint or fracture of the clavicle (62 cases), those of pure obstetric paralysis consisting of trauma to the nerve root, subdivided into paralysis of the upper part of the arm, the lower part of the arm and the whole arm (22 cases) and a mixed group of cases in which both articular damage and injury to the nerve were present (14 cases). In 101 cases of the series there was no record as to the exact type. The classification of these injuries depended on the results of the physical, roentgenographic and electrical examinations of the muscles. The roentgenographic studies showed that in the group of cases of trauma to the joint the normal angle of the head of the humerus as superimposed over the condyles was increased from a position of internal rotation of 20 degrees to an abnormal one of 40 degrees or more. Therefore, with the head of the humerus pointing posteriorly and the whole arm internally rotated, the suprascapular and infrascapular muscles are elongated while the pectoral and subscapularis muscles are contracted. Because of this complicated lesion in the first group of cases, Putti carried out the surgical therapy in two stages. First, a Sever operation was done with severance of the contracted muscles and capsule. The arm was put up in abduction and external rotation for two months. Second, by this approach osteotomy was done through the neck of the humerus, and with elbow flexed at 90 degrees the lower part of the arm was internally rotated to a neutral position. With the arm abducted 45 degrees a second shoulder spica was applied and left on for two months. The treatment in the second group of cases consisted primarily of splinting and physical therapy. Primary nerve sutures were performed in a small series of cases with poor results. The treatment in the third group depended on the site of greatest deformity. The illustrations show excellent operative results in the first group of cases.

[ED. NOTE.—This is a splendid, thorough, long article and is well illustrated. Though previously emphasized by authors, the fact that obstetric paralysis of the shoulder is frequently joint trauma essentially and not pure paralysis is often forgotten. This article merits careful reading, and the therapy suggests trial by others.]

PERIPHERAL VASCULAR DISEASE

Intermittent Venous Occlusion for Treatment of Peripheral Vascular Disease.—Collens and Wilensky¹³ report the effect of treatment in peripheral vascular disease by means of intermittent venous occlusion.

13. Collens, W. S., and Wilensky, N. D.: *The Treatment of Peripheral Obliterative Arterial Diseases*, J. A. M. A. **107**:1960 (Dec. 12) 1936.

They used a pneumatic cuff in the lower third of the femur by means of which from 60 to 80 mm. of mercury was applied in alternating periods of two minutes every two hours. In obliterative disease, e. g., arteriosclerosis, relief is obtained, but treatment must be continued indefinitely. Pain was relieved, ulcers were healed and the walking capacity was increased.

NEOPLASMS

Treatment of Giant Cell Tumors of Bone.—Peirce and Lampe¹⁴ report the results of treatment of 40 patients with giant cell tumor of the bone. Five refused treatment and 6 were treated by preoperative irradiation, surgical intervention and postoperative irradiation, 9 by surgical intervention and postoperative irradiation, 4 by surgical intervention alone and 15 by roentgen irradiation alone. The authors conclude that adequate treatment with roentgen rays or adequate surgical intervention offers as much as the two methods combined. Adequate curettage in anatomically accessible areas has given good functional results. Roentgen treatment offers symptomatic relief and often leads to anatomic repair.

Giant Cell Tumor of the Patella.—Sorge¹⁵ was able to find reports of only 15 cases of giant cell tumor of the patella in the literature. He reports 1 additional case. Treatment consisted in complete removal of the patella and a plastic reconstruction of the quadriceps tendon. The functional and cosmetic results were satisfactory.

Synovial Sarcoma.—Synovial sarcoma is a rare form of malignant tumor of the extremities. Knox¹⁶ reports 3 new cases and includes abstracts of 19 reports in the literature. The tumor arises from a joint, bursa or tendon. It has a characteristic microscopic appearance from which a diagnosis can be made; it is resistant to irradiation. No permanent cure by amputation has yet been recorded.

A series of 117 cases of tumor of the bone in children is presented by Goin and Carroll.¹⁷ In 8.6 per cent the growth was malignant. A classification of bone tumors is offered, in which they are placed in three main groups: (1) those arising from osteogenic elements, (2) those arising from tissues resident in the bone and (3) those of metastatic origin. A review of the characteristics of the various types of tumor of the bone is made, and the results of treatment in the authors' cases are outlined. The writers recommend that a biopsy specimen be secured by aspiration in every case in which a tumor is suspected, and

14. Peirce, C. B., and Lampe, I.: Giant Cell Bone Tumor, J. A. M. A. **107**: 1867 (Dec. 5) 1936.

15. Sorge, E.: Riv. di chir. **2**:399, 1936.

16. Knox, L. C.: Am. J. Cancer **28**:461, 1936.

17. Goin, L. S., and Carroll, R. L.: Radiology **27**:261, 1936.

they offer a plan of approach to the diagnosis of the various types of tumor by roentgen examination.

Hodgkin's Disease with Osseous Involvement.—Dresser and Spencer¹⁸ present a series of 66 cases of Hodgkin's disease with involvement of the bone. The greatest number of these occurred in persons in the third and fourth decades, and the most frequent location was in the spine, pelvis and femur. The incidence of involvement of the bones in Hodgkin's disease as demonstrated roentgenographically is considered to be about 10 per cent, although it is found to be higher at autopsy. Involvement of the bones in Hodgkin's disease is usually considered to occur late, but in 16 of the 66 cases studied the lesions caused the presenting symptoms. The roentgenographic picture usually simulates that of a metastatic malignant process, but it may be confused with the roentgenographic picture of Ewing's tumor, osteogenic sarcoma, bone cyst or osteomyelitis. There is never an entirely characteristic roentgenographic picture; therefore, it must be considered in any unusual lesion. Hodgkin's disease with involvement of the spine often causes collapse of the vertebral body, and when the long bones are involved a pathologic fracture may occur. Involvement of bone may be by direct invasion or by metastasis to the blood stream. Primary Hodgkin's disease of bone has never been observed. The response of the lesion in the bone to irradiation is variable and in general is less satisfactory than that of lesions elsewhere. There is often striking relief from pain, although the prognosis is hopeless. In 36 cases the average duration of life after the first symptoms was three and one-half years; the average duration of life in these cases after the lesion of the bone became evident was eleven months.

Sun Ray Hemangioma of Bone.—Anspach¹⁹ discusses a case of hemangioma of the skull in a child of 11 and then considers the roentgenographic appearance of this type of tumor in different bones. In flat bones a hemangioma usually gives a "sun-ray" or "sunburst" appearance of radiating bone spicules. In proved cases of this tumor in the flat bones there have been strikingly similar patterns. In long bones the sun-ray appearance is not as typical or as constant, and the "soap-bubble" appearance occurs about as frequently. In the spine the predominant features are vertical streaks of parallel densities. The author concludes that although hemangioma is not common it must be suspected in any case of bone tumor showing "sun-ray" spicules, whether occurring in flat or in long bones. No tumor of this sort should be removed without a biopsy first. Treatment should be conservative and consist of roentgen or radium therapy.

18. Dresser, R., and Spencer, J.: *Am. J. Roentgenol.* **36**:809, 1936.

19. Anspach, W. E.: *Sunray Hemangioma of Bone, with Special Reference to Roentgen Signs*, *J. A. M. A.* **108**:617 (Feb. 20) 1937.

MISCELLANEOUS

Ischiopubic Osteochondritis.—Torgersen²⁰ reports 2 instances of ischiopubic osteochondritis in children 8 and 9 years old. Roentgenograms showed slight swelling and sclerosis of the junction between the lower ramus of the pubis and the ischium. The symptom was pain in the inguinal region on walking. The author believes that mechanical factors played a part in causing the lesion. The treatment consisted in preventing overexertion and in correcting static defects. The literature on this lesion is reviewed.

Cervical Rib and Anterior Scalenus Syndrome.—Flothow²¹ reports irritation of the brachial plexus from abnormalities in the supraclavicular triangle. Whether cervical ribs are present or not, section of the anterior scalenus muscle has given relief and is safer than removal of the cervical ribs.

New Roentgenograms of the Skeleton.—Zwerg²² mentions new positions for obtaining valuable roentgenographic information on bones. These are: (1) a transthoracic lateral view of the upper end of the humerus, (2) a transpelvic lateral view of the upper end of the femur, the other hip being flexed 90 degrees to get it out of the field, (3) a lateral view of the cervical portion of the spine, taken at a distance of 6 feet (183 cm.), a flat cassette being used, and (4) a view of the sternum and patella taken with the patient prone rather than supine.

Disk-Shaped Lateral Meniscus with Snapping Knee.—Four cases of disk-shaped lateral meniscus are described by Middleton.²³ He attributes the snapping noise which is associated with movement in this condition to the presence of a ridge dividing the disk into anterior and posterior facets, which contact with the femoral condyle in extension and flexion, respectively. When flexion is being carried out the ridge is pushed back till the movement is almost complete, when it escapes forward with an audible click. The reverse movement of the disk takes place during extension. When the disk-shaped meniscus is fractured, the click takes place over the fractured edge.

Os Acromiale and Its Significance.—The os acromiale has long been recognized by anatomists as an ununited end of the acromium. Schär and Zweifel²⁴ report 22 cases of this anomaly. Occasionally local pain is felt either spontaneously or after trauma. The condition is usually on the right side and is more frequent in the male. Its medicolegal significance lies in its resemblance to an old fracture line. Roentgeno-

20. Torgersen, J.: Norsk mag. f. lægevidensk. 97:951, 1936.

21. Flothow, P. G.: West. J. Surg. 44:570, 1936.

22. Zwerg, H. G.: Arch. f. klin. Chir. 185:578, 1936.

23. Middleton, D. S.: Brit. J. Surg. 24:246, 1936.

24. Schär, W., and Zweifel, C.: Beitr. z. klin. Chir. 164:101, 1936.

grams of the axillary region with the humerus in 90 degrees of abduction reveal the anomaly clearly.

[ED. NOTE.—There is still confusion regarding the diagnosis of this lesion, often by expert roentgenologists. The lesion is not rare, and attention should be called to it.]

Anomalous Bones of Wrist and Foot.—Watkins²⁵ lists and describes 12 anomalous conditions in the wrist and 12 in the foot which might be wrongly considered as due to injuries to these parts. The most important and confusing anomalies in the wrist were congenitally bipartite scaphoids and congenitally ununited styloids of the ulna. In the foot the most important variations were the os trigonum, the tibiale externum (separate and unfused tuberosity of the scaphoid) and a secondary os calcis.

Osteopoikilosis.—Holly²⁶ reports 4 cases of osteopoikilosis. Roentgenograms showed multiple discrete symptomless small areas of increased density in the bones of the extremities. The lesions occurred in a mother, a daughter and two sons, who were studied for five years. The author concludes from his observations that, as previously shown, the disease is familial. The islands of condensation are not constant; in the adult they may entirely disappear. In the child new areas appear with the growth of bone, which may entirely disappear as the child grows or may increase in size as bony development progresses. There is no variation in the uric acid content of the blood or the calcium-phosphorus metabolism.

ORTHOPEDIC OPERATIONS

Tendon Transplantation in Radial Paralysis.—Bonola²⁷ describes 3 cases of old paralysis of the radial nerve in which the treatment consisted of transplantation of tendons from the antagonistic muscles. All of the old operative procedures are reviewed. In the 3 cases described the operation consisted of modified insertion of the flexor carpi radialis longus tendon into the extensor tendons of the thumb and fingers. Usually the flexor carpi ulnaris tendon is inserted into the extensor tendons of the second to the fourth finger and the flexor carpi radialis tendon into the abductor longus and extensor tendons of the thumb. One case is illustrated in which apparently good results were obtained.

Hallux Valgus; Comparison of Two Operations.—Lloyd²⁸ reports 20 cases of bilateral hallux valgus in which different operations were performed on the two sides. On one side the head of the metatarsal

25. Watkins, W. W.: Anomalous Bones of Wrist and Foot in Relation to Injury, J. A. M. A. **108**:270 (Jan. 23) 1936.

26. Holly, L. E.: Am. J. Roentgenol. **36**:512, 1936.

27. Bonola, A.: Chir. d. org. di movimento **22**:239, 1936.

28. Lloyd, E. I.: Brit. J. Surg. **24**:341, 1936.

bone was excised, and on the other, the base of the phalanx and the exostosis of the metatarsal bone. From the patient's replies at the end of from one to three years, it seems there is no choice between the operations as a means of relieving the pain of hallux valgus.

A New Operation for Hallux Valgus.—According to Girdlestone and Spooner,²⁹ hallux valgus consists of valgus of the proximal end of the phalanx and varus of the first metatarsal bone, with splayfoot. The commoner types of operation for hallux valgus are: (1) resection of the head of the first metatarsal bone and (2) hemiphalangectomy, which reduces the deformity but does not improve the splayfoot or the metatarsalgia, if present. These difficulties may appear postoperatively, if not present before. For this reason a new operation was devised, consisting in the removal of the exostosis, removal of the cartilage from the proximal end of the phalanx and removal of all of the phalanx except the very base containing the attachments of the adductor hallucis muscles. This small block of bone is fastened as far medial as possible on the head of the first metatarsal bone with a beef bone peg. This operation improves or prevents splayfoot as well as relieves the hallux valgus and hallux rigidus. Ten of 20 patients with hallux valgus treated by subtotal phalangectomy complained of metatarsalgia and splayfoot postoperatively and 3 complained of them preoperatively. Thirteen of 30 patients who were operated on by the new technic had metatarsalgia preoperatively, but only 1 complained of it postoperatively.

FRACTURES

Metge³⁰ describes an avulsion fracture of the spinous process which occurs while the patient is working. Detachment of the spinous process of the seventh cervical vertebra is the most common form; less commonly the first or second dorsal spinous processes are involved. The lesion occurs when a workman bends his head backward while he is hurling a heavy shovelful of earth upward onto a truck. It has long been described as a clinical syndrome which is often incorrectly diagnosed. Roentgenographic study reveals the lesion if the plates are properly exposed with the lesion in mind. The author finds that excision of the avulsed spinous process results in the quickest and surest recovery.

Anomalies and Fractures of the Vertebral Articular Processes.—Bailey³¹ describes and differentiates between anomalous fissures across the vertebral articular processes and fractures in this region. Anomalous centers of ossification at the tips of the articular processes are more

29. Girdlestone, R. G., and Spooner, H. J.: *J. Bone & Joint Surg.* **19**:30, 1937.

30. Metge, E.: *Deutsche med. Wchnschr.* **62**:1922 (Nov. 20) 1936.

31. Bailey, W.: *Anomalies and Fractures of Vertebral Articular Processes*, *J. A. M. A.* **108**:266 (Jan. 23) 1937.

frequent than commonly supposed. In half the 10 cases described the history of trauma was vague or entirely absent. The defect was often bilateral, and rarely were the superior processes affected. Fracture of the articular process without other injuries to the spine was rare. Pain was prompt and severe, and the fragments were usually displaced.

Ununited Fractures of the Shaft of the Humerus.—The end-results in any large series of ununited fractures treated by operative methods are rarely reported. Campbell³² reports the end-results in 50 cases of ununited fracture of the shaft of the humerus. One patient with an oblique fracture line was treated by transfixion of the fragments with autogenous bone pegs, solid union resulting. The remaining 49 were treated by the application of a massive onlay graft from the tibia secured by autogenous bone pegs. In addition to this, a strip of endosteum was placed within the medulla and bony shavings were placed about the site of the fracture. There were 3 failures in the 49 patients so treated. There were no failures in the 4 patients in whom postoperative infection occurred.

[ED. NOTE.—The results in this series of cases are excellent. The high percentage of successful unions would indicate that this is the method of choice in treating nonunion of the shaft of the humerus and that less secure means of fixation should be discarded.]

Results of Fractures of the Olecranon.—Laukka³³ treated 103 fractures of the olecranon and was able to study the end-results in 56 cases. Five fractures were compound. Loose fragments in the elbow joint were seen in 17 patients. Thirty-five patients were treated by immobilization alone. This was used chiefly in children in whom there was separation of not more than 5 mm. and nothing prevented complete apposition of the fragments. Sixty-five patients were operated on. In most cases stainless steel wire was used to hold the fragments together, and in a few cases, silk. In the follow-up study 10 of 11 patients were found to have less than 20 degrees limitation of motion. Good function was seen in all of these patients. Less than 20 degrees limitation of motion was seen in 22 of 33 patients. Pseudarthrosis was found in 6 patients. Arthritis deformans was frequently seen one or two years after the fracture in 36 per cent of those operated on and in 13 per cent of those treated conservatively. Fracture of the head of the radius was a complication in 7 patients.

Fractures of the Neck of the Femur.—Magnuson³⁴ attempted to evaluate the various methods of treatment used for fracture of the

32. Campbell, W. C.: Ann. Surg. **105**:135, 1937.

33. Laukka, E.: Acta chir. Scandinav. **79**:93, 1936.

34. Magnuson, P. B.: Fracture of Neck of Femur: Evaluation of Various Methods Advanced for Treatment, J. A. M. A. **107**:1439 (Oct. 31) 1936.

neck of the femur. A fracture in this region should be classified according to its line and plane and according to the amount of displacement which originally occurred. When there is considerable obliquity of the fracture line, visual reduction is preferable with immediate fixation. Each patient presents an individual problem. While the Whitman, the Leadbetter and the well leg traction method have their place, internal fixation of the fragments gives greater comfort and makes nursing care easier and the chances of union greater. The author feels that close bony contact, anatomic apposition and absolute fixation are the three most important factors in securing union.

"March Foot."—Elward³⁵ reviews the literature on "March foot" due to foot strain and fracture of a metatarsal bone. He describes two varieties, one due to sudden strain of the foot with fracture of a metatarsal bone and the other due to chronic foot strain and fracture of a metatarsal bone with no definite history of trauma. In the roentgenograms one must differentiate chiefly between sarcoma and Köhler's disease. In the absence of trauma, sarcoma may be suspected, but roentgenograms do not show the "sun-ray" structure. In cases in which the diagnosis is doubtful, weekly roentgenographic examination should make the diagnosis clear. Conservative treatment is indicated.

Fractures of the Neck of the Femur in Childhood.—Mitchell³⁶ reports 10 cases of fracture of the neck of the femur in children. He divides the lesion into three types: (1) epiphysial separation, (2) transcervical fracture and (3) cervicotrochanteric fracture. Bony union practically always occurs, often with coxa vara. The author advises treatment by continuous traction with the hip immobilized in abduction.

Traumatic Separation of the Upper Femoral Epiphysis.—Pfeiffer³⁷ adds 3 cases to the list of cases of traumatic separation of the upper femoral epiphyses during childbirth. The lesion is not easy to recognize. Crepitus is usually absent. Swelling or limitation of motion of the hip generally calls attention to the injury. Careful roentgenographic study will reveal displacement of the intact shaft early and bony callus later. Early recognition, replacement and adequately long fixation are essential if traumatic coxa vara is to be avoided.

Fractures in the New-Born.—A review of the last 6,000 cases of fracture at the Boston Children's Hospital reveals 115 birth fractures, 34 per cent of which were not recognized at the time of their occurrence. In this series the fractures were distributed as follows: fracture of the

35. Elward, J. F.: Am. J. Roentgenol. **36**:188, 1936.

36. Mitchell, J. I.: Fracture of Neck of Femur in Children, J. A. M. A. **107**: 1603 (Nov. 14) 1936.

37. Pfeiffer, R.: Beitr. z. klin. Chir. **164**:18, 1936.

clavicle, 53; of the humerus, 38; of the femur, 20, and of the tibia, 4, including 3 of the fibula also. Unusual obstetric maneuvers were required for 20 per cent of the fractured clavicles, 92 per cent of the fractured humeri, 72 per cent of the fractured femurs and 50 per cent of the fractured tibias. Thorndike and Pierce³⁸ believe that adequate treatment of fractures in the new-born should consist in: (1) early diagnosis, (2) prompt realinement of the fragments (healing is so rapid that after five days it is impossible to reduce the fractures manually), and (3) proper fixation until union has taken place. Methods of treatment are explained in this article: A skein of yarn with figure eight traction is recommended for a fractured clavicle. It was found that in 100 per cent of the cases in which fracture of the femur was treated by strapping the femur to the abdomen the result was unsatisfactory; for this reason an overhead frame with adhesive traction is recommended. Not one instance of true intra-uterine fracture was found in this review. In most cases in this series the fracture occurred in a large baby.

Injection of Alcohol into the Intercostal Nerve in Treatment of Fractures of the Ribs.—Rabboni³⁹ reports 10 cases of fracture of the ribs in which the therapeutic method of Latteri was used. Rabboni states that external splinting does not suffice to immobilize a fractured rib sufficiently to relieve pain and allow normal respiratory movements. If a small amount of alcohol is injected in the vicinity of the corresponding intercostal nerves, nerve block ensues. This is accompanied by complete relief of pain, normal respiration and, without splinting, normal healing of the fractures. If injection into more than two nerves is necessary, the nerves are taken in couples on consecutive days. The procedure of injection consists of inserting the needle at right angles to the under-surface of the rib, and with the needle in contact with the rib it is gently manipulated so that the point is upward just mesial to the inferior ridge of the rib.

[ED. NOTE.—This method of treatment should be used with caution. Unfortunate complications have followed failure to splint broken ribs. Injection into the intercostal nerve is also not without danger.]

Procaine Hydrochloride in the Treatment of Articular Fractures.—In cases of fracture in which there is little or no displacement and in which maintenance of position with apparatus is unnecessary, Leriche and Froehlich⁴⁰ have been starting active motion of the adjacent joint immediately. They first inject 1 per cent procaine hydrochloride into

38. Thorndike, A., and Pierce, F. R.: *New England J. Med.* **215**:1013 (Nov. 26) 1936.

39. Rabboni, F.: *Chir. d. org. di movimento* **22**:263, 1936.

40. Leriche, R., and Froehlich, F.: *Presse méd.* **44**:1665 (Oct. 24) 1936.

the soft tissues about the fracture and if possible into the fracture fissure itself. The effect of this injection lasts for from twelve to twenty-four hours, and the treatment is repeated daily for from two to three weeks. Active motions are repeatedly performed while the parts are under the anesthesia. The authors believe that restoration of function is greatly hastened by this method. In 2 of the reported cases there was gross displacement of the radial head. No attempt was made to reduce or remove the head, but excellent function was obtained in each case by the method described.

[ED. NOTE.—Fracture without displacement and needing no fixation usually gives little trouble however treated. In the foregoing cases of fracture of the head of the radius, both marked displacement and restoration of function without removal of the head seem extraordinary. It does not seem likely that such results could be obtained uniformly.]

RESEARCH

Studies in Healing of Fractures.—Krull⁴¹ studied the problem of healing of fractures with cultures of tissue from chick embryos. At ten days the anlage of the femur was freed from the surrounding tissue. The femur was twisted, and the broken pieces were placed in dishes or flasks containing a mixture of chicken plasma and embryonal extract. Different mineral concentrations and temperatures were investigated. While fibroblastic repair was seen, no calcification or bone production occurred.

Thymus and Bone Regeneration.—Portions of the radius were resected by Haas and Hanke⁴² in rabbits, and healing was observed in a group of animals from which the thymus had been removed. This group did not show any essential difference in bone formation from the control group. The feeding of thymus extract to the animals after the removal of the thymus had no effect either. The rabbits chosen were all growing young animals.

Thyroid Activity and Healing of Fractures.—Eitel and Lexer⁴³ administered thyroid preparations to rabbits. After fracture of the humerus, administration of thyroid was continued, and at various dates the rabbits were anesthetized and mercury was injected into the axillary artery of the fractured extremity. Study of the visualized blood supply of the sites of the fractures indicated that the administration of thyroid caused hyperemia in the area of the callus to occur earlier and that the callus was stronger and lasted longer than in the control animals.

41. Krull, G.: Arch. f. orthop. u. Unfall-Chir. **37**:131, 1936.

42. Haas, A., and Hanke, H.: Deutsche Ztschr. f. Chir. **247**:724, 1936.

43. Eitel, H., and Lexer, E. W.: Arch. f. klin. Chir. **185**:587, 1936.

Influence of the Mineral Constituents of Bone on Ossification.—As a result of carefully controlled animal experimentation, Bisgard⁴⁴ concludes that the synthetic bone salts calcium carbonate, calcium phosphate and magnesium phosphate when locally deposited had no influence on osteogenesis or ossification, whereas bone in the form of partially viable bone, boiled bone or bone ash had a favorable influence on ossification when deposited locally.

Metastases from Tumor Transplants.—Schopper⁴⁵ reports the results of studies on osseous metastases from tumor material injected intravenously into rabbits. The Brown-Pearce⁴⁶ rabbit tumor was used. The rabbits were killed at varying intervals. The metastatic tumors showed best in from three to four weeks. Proliferating tumors were found often as foci without any marked reaction in the surrounding tissue; sometimes there was destruction of bone; rarely was there new bone formation. Tumors were found in the bone marrow and under the periosteum, chiefly in the region of the metaphyses of the long bones. The periosteal tumors were primary transplants and not extensions from the marrow cavity. They stimulated osteophytic activity and at the same time destroyed bone by pressure. New bone formation occurred chiefly by laying down layers of new bone. Rarely was there a metaplasia of the surrounding stroma. No deformities or pathologic fractures were observed.

Study of the Supraspinatus Tendon in Cadavers.—Skinner,⁴⁷ on the basis of dissections on cadavers, presents a description of changes occurring in the supraspinatus tendon in response to continued trauma and to age. It would appear that about 20 per cent of all adult shoulders show some degree of change in the supraspinatus tendon, of which one fourth will show some degree of rupture or splitting. Because of its anatomic relations, the supraspinatus tendon is subject to changes consisting of alteration from fleshy fibers ending in a short tendon to a wide aponeurosis of fibrous tissue blending with the infraspinatus tendon. When this has occurred, because of weakness, splitting, rupture or calcification may follow. Associated changes occur in the greater tuberosity, the intertubercular sulcus, the articular cartilage and the tendon of the long head of the biceps muscle.

Vascularization and Pathologic Structure of the Cotyloid Ligament.—An excellent study of the circulation of the acetabulum is given by Logroscino and Dotti.⁴⁸ The blood supply is derived from the superior

44. Bisgard, J. D.: *Ossification: Influence of Mineral Constituents of Bone*, Arch. Surg. **33**:926 (Dec.) 1936.

45. Schopper, W.: *Virchows Arch. f. path. Anat.* **298**:527, 1937.

46. Domagk, G.: *Centralbl. f. allg. Path. u. path. Anat.* **61**:108, 1934.

47. Skinner, H. A.: *J. Bone & Joint Surg.* **19**:137, 1937.

48. Logroscino, D., and Dotti, E.: *Chir. d. org. di movimento* **22**:285, 1936

and the inferior gluteal vessels and from the obturator. Because of the blood supply, localization or infectious lesions and trophic changes following trauma may be explained.

[ED. NOTE.—This article is too long and full of data to abstract, but it merits reading by all interested in the anatomic and pathologic structure of the acetabulum.]

Ligamentum Teres and Its Vessels.—Schwaiger⁴⁹ studied the ligamentum teres femoris grossly and microscopically at various age periods. He found that vessels could be found in the ligamentum teres up to old age. From the age of 2 years upward there was progressive obliteration of the blood vessels. He believes that the importance of the vessels in the ligamentum teres has been overestimated. No pathologic changes were observed in the cartilage of the upper end of the femur or the surrounding tissues from obliteration of the vessels in the ligamentum teres.

Correlation of Pathologic and Roentgenographic Findings in Tuberculous and Pyogenic Infection of the Vertebrae.—Various authors have assumed that tuberculous or pyogenic hematogenous infection may localize first in the intervertebral disk. Compere and Garrison⁵⁰ point out the fact that the adult intervertebral disk has no blood supply and therefore the disk is never the site of primary infection but is affected by secondary invasion from some adjacent vertebral focus. In a pathologic study of 4 cases of uncomplicated Pott's disease they found that the primary focus was in the vertebral body, either in the centrum or near the epiphysial ring. The disk tissue acted in similar fashion to articular cartilage in other joints and was resistant to destruction. The disease spread by extension beneath the longitudinal ligament and not directly through the disks. The narrowing of the intervertebral space commonly noted seemed to be due to extrusion of the nucleus pulposus through a weakened annulus fibrosus or cartilage plate. In two cases of pyogenic osteomyelitis pathologic examination showed rapid destruction of the adjacent intervertebral disk, as joint cartilage is rapidly destroyed by the proteolytic enzymes in the pyogenic exudate. In contrast to tuberculous infection, regeneration of bone and ankylosis of the vertebral bodies are much more likely to occur in pyogenic infection. The results of microscopic examination in 3 cases of mixed infection (tuberculous plus pyogenic) of the spine were reported.

Rôle of the Reticulo-Endothelial System in the Deposition of Colloidal Matter in Articular Cavities.—In studying the rôle of the reticulo-endothelial system in the deposition of colloids and particulate

49. Schwaiger, M.: Ztschr. f. Orthop. 65:297, 1936.

50. Compere, E. L., and Garrison, M.: Ann. Surg. 104:1038, 1936.

matter in articular cavities, Kuhns and Weatherford⁵¹ used rats into which they injected trypan blue subcutaneously or by gavage. Various series of experiments were made in an attempt to exclude the rôle of the lymphatics. In conclusion, the authors found that colloidal and particulate matter was carried to the articular cavities from the various tissues of the body, such as the skin and the gastro-intestinal tract, through the blood stream. This material was stored chiefly in histiocytes in the synovial membrane, in the bone marrow and in lesser amounts in the intermuscular septums and in the articular fat pads. Mild inflammation in articular tissues tended to increase the amount of deposition of such transplanted substances. Local blocking of the reticulo-endothelial system was transitory and incomplete and was not effective in preventing the deposition of colloidal and particulate matter in articular tissue.

Auscultation of Joints.—Steindler⁵² stresses the importance of auscultation in the examination of joints. He presents a preliminary report based on the auscultatory findings in a series of 397 knee joints. The instruments used were the stethoscope, the cardiophone and the oscillograph. The interpretation of sound phenomena is difficult because extraneous and extra-articular noises must be differentiated from the intra-articular noises. However, certain sounds can be considered intra-articular because of their character and the regularity of their occurrence. Sustained grating in all quadrants of the knee joint indicates general involvement of the joint with arthritic changes which may or may not be the background of isolated internal derangements. Isolated sounds are cracks, clicks and thuds. High-pitched cracks indicate a hard body, such as a joint mouse, while lower-pitched clicks and thuds indicate softer bodies, such as fringes and semilunar cartilages. The author does not claim to be able to make definite diagnosis by auscultation but feels that it is of aid in locating the lesion inside the joint.

51. Kuhns, J. G., and Weatherford, H.: Rôle of Reticulo-Endothelial System in Deposition of Colloidal and Particulate Matter in Articular Cavities, *Arch. Surg.* **33**:69 (July) 1936.

52. Steindler, A.: *J. Bone & Joint Surg.* **19**:121, 1937.

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INCIDENCE OF ASYMPTOMATIC PATHOLOGIC CONDITIONS OF THE APPENDIX

BASED ON A STUDY OF 2,065 CONSECUTIVE INCIDENTAL
APPENDECTOMIES

HAROLD J. SHELLEY, M.D.

Assistant Attending Surgeon and Chief of Surgical Clinic, St. Luke's Hospital
NEW YORK

This paper is based on a study of the records of 2,065 consecutive incidental appendectomies performed at St. Luke's Hospital in the period between 1925 and 1935 inclusive. The word incidental as used here refers to those appendectomies performed during abdominal operations, the indications for which were in no way associated with the appendix. None is included which was performed when present or past disease of the appendix was suspected before operation. Doubtless some of the patients may have had appendical symptoms at some time in the past, but neither the history nor the physical findings suggested any pathologic condition of the appendix.

Originally this analysis was undertaken to obtain a standard for comparison with the pathologic conditions found in appendixes removed because of symptoms attributed to chronic appendicitis. By selecting the material as previously noted and then eliminating all in which any inflammatory condition was present elsewhere in the abdomen, the resultant figures should approximate closely the expected incidence of pathologic changes in the appendix when it is not the cause of the patient's symptoms. In obtaining the set of figures just described, other statistics were obtained which appeared to be of considerable interest. This paper was written to present these figures.

So far as possible, everything was excluded which pertained to a primary operation, and attention was centered on the results of the study of the appendixes. In order to do this, the incidences were calculated on the total number of appendixes in each group under consideration at the time and not on the total number in the whole series. In this way comparisons have been made in which the effect of the indications for the primary operations were largely, if not entirely, eliminated.

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REGION OF THE PRIMARY OPERATION

The data in table 1 are given only to show how the primary operations were distributed in regard to the operative region. A detailed list of the operations was felt to be too complicated, particularly as from 2 to 6 different operative procedures other than appendectomy were performed on many of the patients. There is an apparent increase of 110 operations over the total of 2,065, because in some instances the primary operative procedures were done on the same patient in two different regions. Additional operative procedures outside of the abdomen, of which there were a considerable number, were not listed.

The mortality for each group did not appear to be above the normal expectancy, with but one exception. This was for the operations performed for some condition associated with the colon. A careful study of this material and of the causes of death shows that the mortality was not above the normal expectancy, although this does not obviate the fact that it was unwise to add an appendectomy to the primary operation, which was imperative.

TABLE 1.—*Distribution of Primary Operations According to the Operative Region, With Mortality for Each Group**

Operative Region	Number of Operations	Number of Deaths	Mortality, Percentage
Female generative organs.....	1,654	13	0.79
Gallbladder and liver.....	312	5	1.61
Hernia.....	68	0	0.00
Stomach and duodenum.....	53	2	3.77
Colon.....	17	5	29.82
Small intestine.....	6	0	0.00
Other intra-abdominal regions.....	65	2	3.07

* The total number of primary operations is increased to 2,175 because often a "primary" operation was done in more than one region on the same patient. When more than one operative procedure was performed in one region they are listed as one operation. Additional operative procedures not involving the abdominal cavity are not listed.

INCIDENCE OF PATHOLOGIC CONDITIONS IN THE APPENDIX

Table 2 lists the pathologic conditions in the appendixes, their incidence (calculated on 1,904 examined microscopically) and the mortality for each group.

No microscopic examination was made of 161 appendixes. Of those examined, 14 showed conditions other than a nonspecific inflammation. These, together with 7 which showed some pathologic process in addition to a nonspecific inflammation, will be considered in tables 13 and 14. The latter 7 are also listed in their proper place according to the inflammatory change.

This leaves 1,890 appendixes which formed the basis for the figures in tables 3 to 12 and in charts 1 to 16. A brief definition of the various types of inflammatory change is given. They have been listed

separately throughout the tables, as it was felt that the term chronic appendicitis was too ambiguous.

No Definite Evidence of Inflammation.—In 702 appendixes no definite evidence of inflammation was found. These made up 37 per cent of the group now being discussed. They were divided pathologically into the two classes listed here.

Normal Appendixes: All appendixes which appeared normal or relatively normal with no definite pathologic change were listed as normal. There were 629 appendixes, or 33 per cent of the total, in this group.

Atrophic Appendixes: The wall of an atrophic appendix is very thin and shows no definite evidence of inflammation. This condition is due largely to pressure from within the appendix, present over an appreciable period of time. Seventy-three appendixes, 4 per cent of the total, showed this pathologic change.

Definite Inflammatory Changes.—As contrasted to the appendixes with no definite evidence of inflammation, 1,188, or 62 per cent of the 1,890 being discussed, showed definite inflammatory change. These have been divided into two main groups according to the degree of the inflammatory change present.

Simple Chronic Appendicitis: In this group were placed those appendixes showing a definite, but not marked, evidence of chronic inflammation throughout the various parts of the wall or only in the mucosa and submucosa. This lesion was found in 573 appendixes, or 48 per cent of those showing inflammatory change (30 per cent of the total group).

Marked Inflammatory Changes: As contrasted to the foregoing group, a more extensive inflammatory lesion was found in 615 appendixes, or 52 per cent of those showing inflammatory change (32 per cent of the total group). The various types of conditions which this included will be discussed.

Chronic catarrhal appendicitis is characterized by a moderate degree of chronic inflammation in the mucosa and submucosa, with definite catarrhal changes in the mucosa and usually a slight infiltration in the muscle. This lesion was found in 82 appendixes, or 13 per cent of those showing marked changes (4 per cent of the total group).

Chronic exudative appendicitis is a definite pathologic lesion which is often seen as a late stage in the recovery from an attack of acute appendicitis. It is characterized, as the name indicates, by a marked chronic exudative process. There is a dense extensive infiltration with the various cells typical of chronic inflammation, and often chronic edema is present. The lumen of the appendix, the blood vessels and the perivascular tissues frequently contain some polymorphonuclear leukocytes. This lesion was found in 157 appendixes, or 26 per cent of those showing marked changes (8 per cent of the total group).

Acute appendicitis, which requires no definition, was found in 33 appendixes, or 5.4 per cent of those which showed marked changes (2 per cent of the total group). An acute suppurative process was present in 6, an acute and acute catarrhal process in 12 and a subacute process in 15. The subacute process lies between acute and chronic exudative appendicitis.

The records of the patients from whom the foregoing 33 appendixes were removed were rechecked for any history or physical findings which would even suggest the possibility of appendical disease at the time of the operation or previously. None could be found. Three of the acute suppurative appendixes were removed from my own personal patients. In each instance, after the pathologic changes were reported the history was rechecked with the patient. No overlooked points in the history which pointed in any way to the presence of appendicitis were disclosed.

One must bear in mind the possibility that the pathologic changes present in some of the appendixes which presented acute or subacute, but not suppurative, inflammation might have been produced by the appendix having been packed away tightly with pads while a long primary operation was being performed.

Chronic obliterative appendicitis with infiltration likewise requires no definition, as the name gives a complete description of the pathologic lesion. The mucosa and often the other coats, even including a part of the muscle, have disappeared and been replaced by granulations or scar tissue, which, with the muscle, shows a definite infiltration. The process may involve a part of or the whole appendix. It probably represents either a stage in the healing of a suppurative or ulcerative process or a renewed inflammation in an appendix which had previously healed. This condition was observed in 106 appendixes, or 17 per cent of those showing marked changes (6 per cent of the whole group).

Chronic obliterative appendicitis without infiltration is, as the name designates, the same as the foregoing condition with the exception that it is a completely healed process without inflammation. One hundred and eighty-three appendixes were so effected, or 30 per cent of those showing marked pathologic changes (10 per cent of the total group). Of the 7 groups of appendixes which presented marked inflammatory changes, this was the largest.

Chronic periappendicitis is associated with and due to a chronic inflammatory lesion elsewhere in the abdomen, usually chronic salpingitis. This pathologic condition was present in 31 appendixes, or only 5 per cent of those showing marked changes (2 per cent of the total group). The number was surprisingly small considering the large number of cases of salpingitis included in the list.

Acute periappendicitis constitutes its own definition. This condition is associated with and due to an acute inflammatory lesion elsewhere in the abdomen. It was found in only 23 appendixes, or 3.7 per cent of those which showed marked changes (1 per cent of the total group). This group was small because ordinarily the primary lesion in the abdomen and the patient's condition were contraindications to doing an incidental appendectomy.

MORTALITY ACCORDING TO CONDITION FOUND IN THE APPENDIX

The mortality figures are given only for completeness. The pathologic condition found in these appendixes had no bearing on any of the

TABLE 2.—*Classification of Pathologic Conditions of Appendixes, With the Incidence and Mortality for Each Group*

Condition in Appendix	Number of Appendixes	Percentage*	Number of Deaths	Mortality, Percentage
No microscopic examination.....	161	1	0.62
Mucocele.....	3	0.16	0	0.00
Tuberculosis.....	5	0.26	1	20.00
Tumor.....	6	0.32	0	0.00
No inflammation.....	702	36.9	5	0.71
Normal.....	629	33.1	4	0.62
Atrophic.....	73	3.8	1	1.37
Inflammation.....	1,188	62.4	20	1.67
Simple chronic appendicitis.....	573	50.1	10	1.75
Marked inflammatory changes.....	615	52.3	10	1.63
Chronic catarrhal appendicitis....	82	4.3	1	1.22
Chronic exudative appendicitis....	157	8.3	2	1.27
Acute appendicitis.....	33	1.7	0	0.00
Chronic obliterative appendicitis with infiltration.....	106	5.6	1	0.94
Chronic obliterative appendicitis without infiltration.....	183	9.6	4	2.19
Chronic periappendicitis.....	31	1.6	0	0.00
Acute periappendicitis.....	23	1.2	2	8.70
Totals.....	2,065	100.00	27	1.31

* The percentages are calculated only on the 1,904 appendixes examined microscopically.

deaths in this list. Any increase above the average is due to the primary operation or to the indication for that operation.

The number of tuberculous appendixes was too small for the mortality percentage to be significant. The single death was due to generalized tuberculosis.

Chronic obliterative appendicitis with infiltration is found to a large extent in older patients. They are poorer operative risks and more often require extensive primary operations for more serious conditions than younger patients. Possibly this argues that they should not undergo an incidental appendectomy, although the mortality for the group reported here is no greater than would be expected had the appendectomy not been done.

The increase in mortality in the group of patients with acute periappendicitis was caused by the death of 2 with advanced generalized

peritonitis due to a perforated diverticulum of the sigmoid colon. Undoubtedly these patients should not have been subjected to an appendectomy.

RELATION OF INFLAMMATORY CHANGE IN THE APPENDIX TO INFLAMMATION ELSEWHERE IN THE ABDOMEN

The relationship of inflammatory change in the appendix to inflammation elsewhere in the abdomen, without taking into consideration the type or location of the latter, is shown in table 3. This and all subsequent percentage charts have been so arranged that comparisons may be made by reading down the columns of percentages. Any effect that

TABLE 3.—*Relation of the Inflammatory Change in the Appendix to the Incidence of Inflammation Elsewhere in the Abdomen **

Condition in Appendix	Total Appendixes	Condition Elsewhere in Abdomen			
		No Inflammation		Inflammation	
		Number	Percentage	Number	Percentage
No inflammation.....	702	465	66.2	237	33.8
Normal.....	629	415	66.0	214	34.0
Atrophic.....	73	50	68.5	23	31.5
Inflammation.....	1,188	674	56.8	514	43.2
Simple chronic appendicitis.....	573	320	55.8	253	44.2
Marked inflammatory changes.....	570	354	62.1	216	37.9
Chronic catarrhal appendicitis.....	82	55	67.0	27	33.0
Chronic exudative appendicitis.....	157	94	59.8	63	40.2
Acute appendicitis.....	33	23	69.7	10	30.3
Chronic obliterative appendicitis with infiltration.....	106	59	55.7	47	44.3
Chronic obliterative appendicitis without infiltration.....	183	119	65.0	64	35.0
Chronic periappendicitis.....	31	4	12.9	27	87.1
Acute periappendicitis.....	23	0	00.0	23	100.0
Totals.....	1,890	1,130	60.3	751	39.7

* For comparisons read the vertical percentage columns. This table is elaborated in tables 4 and 5.

the items listed on the left had on the items listed at the top of the table are shown by variations in the vertical columns of figures.

The distribution of the appendixes according to the various types and locations of inflammation elsewhere in the abdomen is presented in table 4, and the corresponding incidences, figured on the total number of appendixes listed under each type of pathologic condition found elsewhere in the abdomen, in table 5. A slight increase in the incidence of appendixes showing inflammatory change accompanied the presence of inflammation elsewhere in the abdomen. This increase was greatest in the groups of appendixes affected with periappendicitis. Here, of course, the cause of this increase was elsewhere than in the appendix, and the relation is self-evident.

No cases of acute appendicitis were included under the headings chronic suppurative and acute salpingitis. In looking up the records, 30

TABLE 4.—*Distribution of Appendices According to the Various Types of Inflammation Occurring Simultaneously Elsewhere in the Abdomen*

Condition in Appendix	Condition Elsewhere in Abdomen											
	No Inflammation	Inflammation	Saphngitis	Chronic Saphngitis	Chronic Suppurative Saphngitis	Acute Saphngitis	Cholecystitis	Peptic Ulcer	Tuberculous Peritonitis or Saphngitis	Peritonitis	Other Types of Inflammation	Total Appendices
No inflammation.....	465	237	145	125	9	11	71	13	3	1	1	702
Normal.....	415	211	135	115	9	11	63	12	2	1	1	629
Atrophic.....	50	23	10	10	0	0	11	1	1	0	0	73
Inflammation.....	671	514	306	292	50	51	161	29	5	0	7	1,188
Simple chronic appendicitis.....	320	253	118	105	30	13	80	13	5	3	4	573
Marked inflammatory changes.....	351	261	158	97	20	11	81	16	0	3	3	615
Chronic catarrhal appendicitis.....	55	27	20	16	1	3	7	0	0	0	0	82
Chronic exudative appendicitis.....	91	63	39	27	2	10	18	5	0	0	1	157
Acute appendicitis.....	23	10	2	2	0	0	7	0	0	1	0	33
Chronic obliterative appendicitis with inflammation.....	59	17	19	13	2	1	19	7	0	0	2	166
Chronic obliterative appendicitis without inflammation.....	119	61	50	25	2	3	30	1	0	0	0	183
Chronic periaependicitis.....	1	27	27	13	13	1	0	0	0	0	0	31
Acute periaependicitis.....	0	23	21	1	0	20	0	0	0	2	0	23
Totals.....	1,139	751	451	327	59	65	235	12	8	7	8	1,890

TABLE 5.—*Distribution of Appendices According to Various Types of Inflammation Occurring Simultaneously Elsewhere in the Abdomen*
(Percentages) *

Condition in Appendix	Total Appen- dixes	No Inflam- mation	Condition Elsewhere in Abdomen									
			Inflam- mation	Salpin- gitis	Chronic Salpin- gitis	Chronic Suppur- ative Salpin- gitis	Acute Salpin- gitis	Chole- cystitis	Peptic Ulcer	Tuberculous or Salpin- gitis	Peri- tonitis	Other Types of Inflam- mation
No inflammation.....	702	66.24	33.76	20.65	17.81	1.28	1.56	10.45	1.85	0.44	0.14	0.14
Normal.....	629	65.97	34.03	21.46	18.28	1.43	1.75	10.02	1.91	0.32	0.16	0.16
Atrophic.....	73	68.49	31.51	13.69	13.69	0.00	4.55	15.07	1.37	1.37	0.00	0.00
Inflammation.....	1,188	56.73	43.27	25.76	17.00	4.21	2.27	13.55	2.44	0.43	0.50	0.00
Simple chronic appendicitis.....	573	55.85	44.15	25.83	18.32	5.23	6.67	13.96	2.27	0.87	0.52	0.39
Marked inflammatory changes.....	615	57.56	42.44	25.76	15.77	3.25	3.66	13.17	2.60	0.00	0.49	0.70
Chronic catarrhal appendicitis.....	82	67.07	32.93	24.39	19.51	1.22	6.37	8.54	0.00	0.00	0.00	0.49
Acute exudative appendicitis.....	157	59.87	40.13	24.83	17.19	1.27	0.00	11.47	3.19	0.00	0.00	0.00
Chronic obliterative appendicitis.....	33	69.70	30.30	6.06	6.06	0.00	0.00	21.21	0.00	0.00	0.00	0.64
Chronic obliterative appendicitis with infiltra- tion.....	106	55.63	44.34	17.92	12.26	1.89	3.77	17.92	6.61	0.00	3.93	0.00
Chronic obliterative appendicitis without infl- tration.....	183	65.03	34.97	16.39	13.66	1.09	1.64	16.39	2.19	0.00	0.00	1.89
Acute periappendicitis.....	31	12.90	87.09	41.93	41.93	41.93	3.23	0.00	0.00	0.00	0.00	0.00
.....	23	0.00	100.00	91.30	4.35	0.00	86.96	0.00	0.00	0.00	8.70	0.00
Figures for whole group.....	1,800	60.26	39.74	23.86	17.30	3.12	3.44	12.43	2.22	0.43	0.37	0.43

* The percentage incidence was calculated on the total number of appendices classified with each type of pathologic condition found elsewhere in the abdomen. For comparisons, read the vertical columns.

cases were found in which subacute, acute or acute suppurative appendicitis occurred simultaneously with one of these two conditions when the indication for the operation was a pathologic condition of the tubes. However, they were all discarded as it was impossible to state positively that the symptoms were not at least partially due to the inflammatory process in the appendix.

One portion of this table is interesting because of the definite lack of relationship shown and will be taken up in detail later.

RELATION OF INFLAMMATORY CHANGE IN THE APPENDIX TO INFLAMMATION IN THE GALLBLADDER

The statement has often been made that inflammation in the gallbladder is largely, or at least frequently, caused by a chronic inflam-

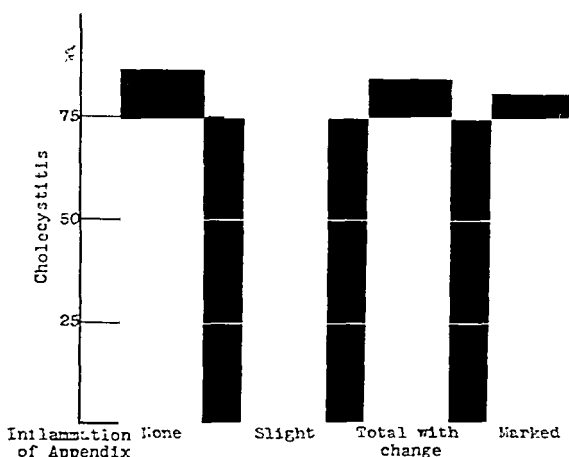


Chart 1.—Relation of inflammatory change in the appendix to the incidence of inflammation in the gallbladder. The incidence of the latter does not increase in the presence of inflammatory change in the appendix.

matory process in the appendix. Tables 6 and 7 and charts 1 and 2 present the statistics for cases in which the gallbladder and appendix were removed simultaneously. If inflammation in the appendix causes inflammation in the gallbladder, the incidence of cholecystitis should show a definite increase when inflammation is found in the appendix, and one might expect that increase to be greater the more marked the inflammatory change in the appendix. The tables and charts do not show this. In fact, there is a slight variation in the opposite direction (table 6 and chart 1). Conversely, the incidence of normal gallbladders should be decreased in the presence of inflammatory change in the appendix. As before, a slight variation in the opposite direction is found (table 6 and chart 2).

The same relation is presented in table 7, but the incidence of inflammatory change in the appendix was calculated on the number of normal gallbladders and those showing cholecystitis. The same lack of causative relationship is seen.

A careful examination of these figures discloses no evidence to substantiate the statement that chronic inflammation in the appendix causes inflammation in the gallbladder.

TABLE 6.—*Relation of Inflammatory Change in the Appendix to Inflammation in the Gallbladder **

Condition in Appendix	Total Appen- dixes	Condition in Gallbladder			
		Normal		Cholecystitis	
		Num- ber	Per- centage	Num- ber	Per- centage
No inflammation.....	86	12	13.9	74	86.1
Inflammation.....	190	29	15.3	161	84.7
Slight.....	90	10	11.1	80	88.9
Marked.....	100	19	19.0	81	81.0
Totals.....	276	41	14.8	235	85.2

* This table indicates that inflammation in the appendix is not a cause of inflammation in the gallbladder. If it were, an increase in the incidence of cholecystitis should be found in the presence of inflammatory change in the appendix. There is instead a slight decrease in incidence. This table is shown graphically in charts 1 and 2.

TABLE 7.—*Relation of Inflammation in the Gallbladder to Inflammatory Change in the Appendix **

Condition in Gallbladder	Total Cases	Inflammatory Change in Appendix							
		None		Total		Slight		Marked	
		Num- ber	Per- centage	Num- ber	Per- centage	Num- ber	Per- centage	Num- ber	Per- centage
Normal.....	41	12	29.1	29	70.9	10	24.4	19	46.5
Cholecystitis.....	235	74	31.5	161	68.5	80	34.2	81	34.3
Totals.....	276	86	31.1	190	68.9	90	32.6	100	36.4

* This table indicates that in the presence of inflammation in the gallbladder there is no increase in the incidence of inflammatory change in the appendix.

RELATION OF INFLAMMATION ELSEWHERE IN THE ABDOMEN TO INFLAMMATORY CHANGE IN THE APPENDIX

The distribution of inflammatory conditions in the abdomen and their proportionate frequency, without taking into consideration the type of inflammatory change in the appendix, is presented in table 8. The distribution is shown in detail in table 9, and the corresponding incidences, calculated on the total number of cases in each group, in table 10.

By reading down the percentage columns in table 10 under each type of pathologic process found in the appendix, the effect, if any, on each pathologic process of inflammation elsewhere in the abdomen can be readily seen. An extensive discussion is unnecessary.

In the presence of inflammation elsewhere in the abdomen there was a definite increase in the incidence of inflammatory change in the appendix. This same relation held true with simple chronic appendicitis, marked inflammatory changes (total), chronic obliterative appendicitis with infiltration and, as one would expect, to a much greater extent with chronic and acute periappendicitis. No causative relationship was indicated in chronic catarrhal appendicitis, chronic exudative appendicitis, acute appendicitis and chronic obliterative appendicitis without infiltration. Apparently inflammation elsewhere in the abdomen has no appreciable effect on any of the latter group of changes found in the appendix. The only really outstanding relationship shown was that of salpingitis and peritonitis in causing acute and chronic periappendicitis.

What appears to be an abnormal variation under chronic obliterative appendicitis (both groups) was due to what is later shown to be age incidence. Here the higher percentages were found in those conditions

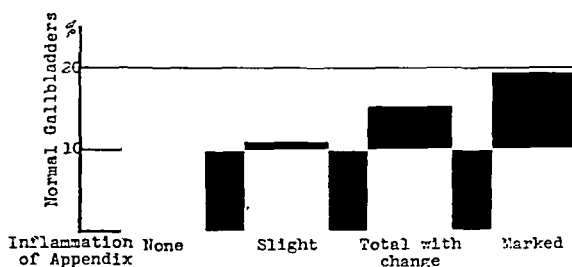


Chart 2.—Relation of inflammatory change in the appendix to the incidence of normal gallbladders. The incidence of the latter does not decrease in the presence of inflammatory change in the appendix.

occurring chiefly in middle and later life and the low percentages in conditions found in the early decades of life. This same relationship can be seen to a lesser degree in other parts of this table.

INCIDENCE OF INFLAMMATORY CHANGE IN THE APPENDIX ACCORDING TO AGE

In discussing the relationship of inflammatory change in the appendix to age, the age groups from 1 to 10 and from 71 to 80 will be ignored because of the small number of patients in each. The total number in groups from 11 to 20 and from 61 to 70 were much smaller than in those remaining, but, since there are sufficient to figure percentages and in each the resultant figures fell well within the expected percentages, they have been used without weighting.

The incidence of the total number of appendixes showing inflammatory changes increased definitely with age. However, the incidence

of those showing the various types of inflammation varied considerably from that in the total group. These differences are shown graphically in charts 3 to 16.

The increase of incidence of the appendixes with inflammatory change which occurred with an increase in age and the corresponding decrease in the number of appendixes without inflammatory change can be seen in chart 3 (solid lines). A more uniform decrease with age through the middle decades was found by eliminating the atrophic appendixes and considering only the normal appendixes. When the atrophic appendixes were added to those showing inflammatory change,

TABLE 8.—*Effect of Inflammation Elsewhere in the Abdomen on the Incidence of Inflammation in the Appendix**

Condition Elsewhere in Abdomen	Total Cases	Condition in Appendix			
		No Inflammation		Inflammatory Change	
		Num-ber	Per-centage	Num-ber	Per-centage
No inflammation.....	1,139	465	40.8	674	59.2
Inflammation.....	751	237	31.6	514	68.4
Salpingitis.....	451	147	32.1	306	67.9
Chronic salpingitis.....	327	125	38.2	202	61.8
Chronic suppurative salpingitis.....	59	9	15.2	50	84.8
Acute salpingitis.....	65	11	18.5	54	81.5
Cholecystitis.....	235	74	31.5	161	68.5
Peptic ulcer.....	42	13	30.9	29	69.1
Tuberculous peritonitis or salpingitis.....	8	3	37.5	5	62.5
Peritonitis.....	7	1	14.3	6	85.7
Other types of inflammation.....	8	1	12.5	7	87.5
Totals.....	1,890	702	37.1	1,188	62.9

* For comparisons, read the vertical percentage columns. Apparently the incidence of inflammation in the appendix is increased slightly by the presence of inflammation elsewhere in the abdomen. This table is elaborated in tables 9 and 10.

a correspondingly more uniform increase of the changes in the appendix with age was obtained (broken lines). This is a better representation of the effect of age on the appendix.

The incidence of the total number of appendixes without inflammation decreased gradually with age (chart 4). The decrease in the incidence of normal appendixes was slightly more marked (chart 5). The increase in the incidence of atrophic appendixes with an increase in age is represented in chart 6.

The incidence of the total number of appendixes showing inflammatory change increased with age (chart 7). However, there was a fairly stationary period during middle life. The trend or complete lack of trend is much more definitely seen in the various groups which make up this total.

TABLE 9.—*Distribution of the Various Types of Inflammation Found in the Appendix According to the Type of Inflammation Found Elsewhere in the Abdomen*

Condition Elsewhere in Abdomen	Condition in Appendix													Total Cases
	No Inflammation	Normal	Atrophic	Inflammation	Simple Chronic Appendicitis	Marked Inflammatory Changes	Chronic Catarrhal Appendicitis	Chronic Exudative Appendicitis	Chronic Obliterative Appendicitis			Chronic Perforative Appendicitis		
									Acute Appendicitis	Without Infiltration	With Infiltration			
No inflammation.....	465	415	50	674	320	354	55	91	23	50	119	4	0	1,130
Inflammation.....	237	211	23	514	253	201	27	63	10	47	64	27	23	751
Salpingitis.....	145	135	10	306	148	168	20	39	2	10	30	27	21	451
Chronic salpingitis.....	125	115	10	292	105	97	16	27	2	13	25	13	1	327
Chronic suppurative salpingitis.....	9	0	0	50	30	20	1	2	0	2	2	13	0	50
Acute salpingitis.....	11	11	0	51	13	41	3	10	0	4	3	1	20	65
Cholecystitis.....	74	63	11	101	80	81	7	18	7	19	30	0	0	235
Peptic ulcer.....	13	12	1	29	13	16	0	5	0	7	4	0	0	42
Tuberculous peritonitis or salpingitis..	3	2	1	5	5	0	0	0	0	0	0	0	0	8
Peritonitis.....	1	1	0	6	3	3	0	0	1	0	0	0	2	7
Other types of inflammation.....	1	1	0	7	4	3	0	1	0	2	0	0	0	8
Total appendices.....	702	620	73	1,188	573	615	82	157	33	103	183	31	23	1,890

TABLE 10.—*Distribution of the Various Types of Inflammation Found in the Appendix According to the Type of Inflammation Found Elsewhere in the Abdomen (Percentages) **

Condition Elsewhere In Abdomen	Total Cases	Condition in Appendix												
		No Inflammation	Normal	Atrophic	Inflammation	Simple Chronic Appendi- citis	Marked Inflam- matory Changes	Chronic Catar- rhal Appendi- citis	Chronic Exuda- tive Appendi- citis	Chronic Obliterative Appendicitis				
										Acute Appendi- citis	With Infltra- tion	Without Infltra- tion	Chronic Peri- appendi- citis	
No Inflammation.....	1,139	40.82	36.52	4.30	50.18	28.10	31.10	4.83	8.25	2.02	5.18	10.45	0.35	0.00
Salpingitis.....	751	31.56	28.50	3.06	68.44	33.69	34.75	3.59	8.39	1.33	6.26	8.52	3.59	3.06
Chronic salpingitis.....	451	32.15	20.94	2.21	67.85	32.82	35.03	4.21	8.63	0.44	4.21	6.65	5.99	4.65
Chronic suppurative salpin- gitis.....	327	38.22	35.32	2.00	61.78	32.12	29.66	4.90	8.30	0.62	3.98	7.65	3.98	0.32
Acute salpingitis.....	59	15.25	15.25	0.00	84.75	50.85	33.90	1.69	3.39	0.00	3.39	3.39	22.03	0.00
Cholecystitis.....	65	18.46	18.46	0.00	81.54	18.46	63.08	4.02	14.62	0.00	6.15	4.62	1.51	29.24
Peptic ulcer.....	235	31.49	26.81	4.68	68.51	34.04	34.47	2.98	7.67	2.98	8.09	12.77	0.00	0.00
Tuberculous peritonitis or salpingitis.....	42	30.95	28.27	2.38	69.05	30.96	38.09	0.00	11.90	0.00	16.67	9.52	0.00	0.00
Peritonitis.....	8	37.50	25.00	12.50	62.50	62.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Other types of Inflammation..	7	14.29	14.29	0.00	85.71	42.85	42.85	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Figures for whole group...	8	12.50	12.50	0.00	87.50	37.50	37.50	0.00	12.50	0.00	25.00	0.00	0.00	0.00
	1,890	37.15	33.28	3.87	62.85	30.31	32.54	4.34	8.31	1.75	5.61	9.68	1.61	1.22

* The percentage incidence was calculated on the total number of appendixes classified with each type of inflammation elsewhere in the abdomen. For com-
parisons, read the vertical columns.

* The percentage incidence was calculated on the total number of appendices classified with each type of inflammation elsewhere in the abdomen. For com-
parisons, read the vertical columns.

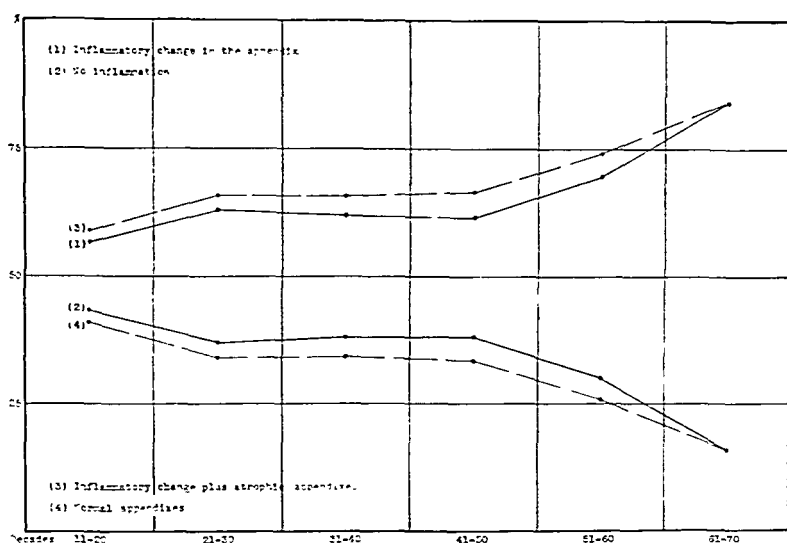


Chart 3.—The effect of age on the incidence of changes in the appendix. The comparison is shown of no inflammation to inflammatory change (solid lines) and also of normal appendixes to those showing atrophic and inflammatory change (broken lines).

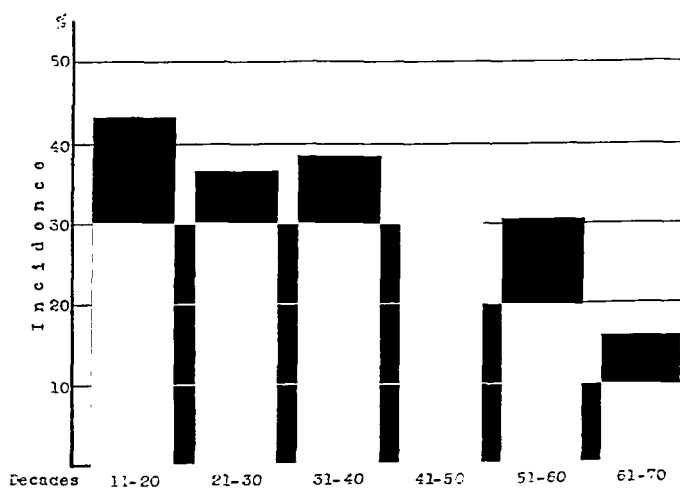


Chart 4.—Incidence of appendixes which presented no inflammatory change according to age.

There was a slight but definite decrease in the incidence of simple chronic appendicitis with age (chart 8). This might be accounted for by the fact that appendixes with more marked pathologic processes as age increases come from this group as well as from the group of normal appendixes. The total number of appendixes with marked changes

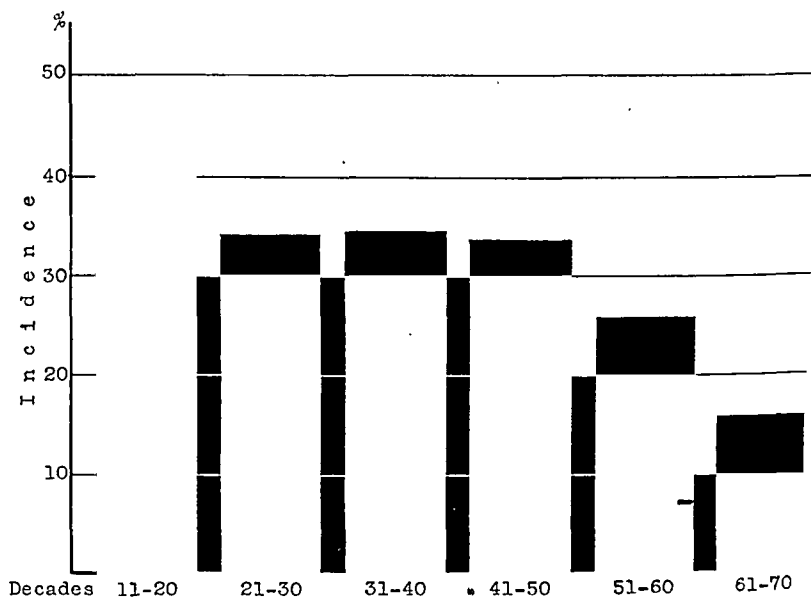


Chart 5.—Incidence of normal appendixes according to age. Those appendixes which were relatively normal, i. e., showed no definite inflammatory change, were also included.

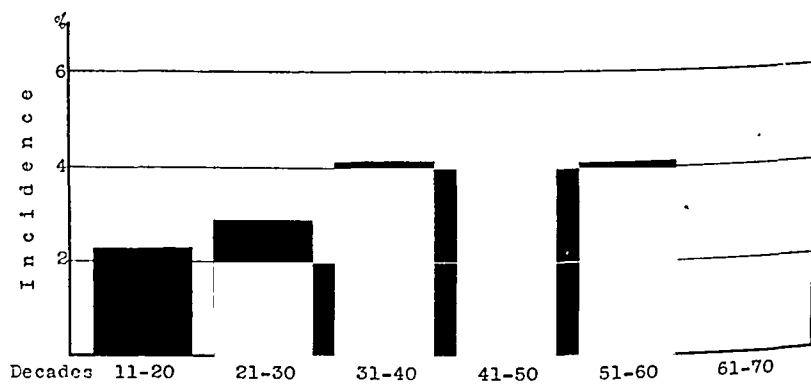


Chart 6.—Incidence of atrophic appendixes according to age.

increased in incidence with age (chart 9). There was a slight increase in the incidence of chronic catarrhal appendicitis with an increase in age (chart 10). There was a marked increase with age in the incidence of chronic obliterative appendicitis, both with (chart 11) and without infiltration (chart 12). The incidence of chronic exudative appendicitis (chart 13) and acute appendicitis (chart 14) showed a spread

throughout, indicating that age had no effect. This is of particular interest as pathologically these conditions are closely related.

There was an increase in the incidence of periappendicitis, both chronic (chart 15) and acute (chart 16), in the early age group and a marked decrease with age. This is exactly as would be expected, because, as mentioned earlier, the causes of periappendicitis are largely conditions occurring in early and early middle life.

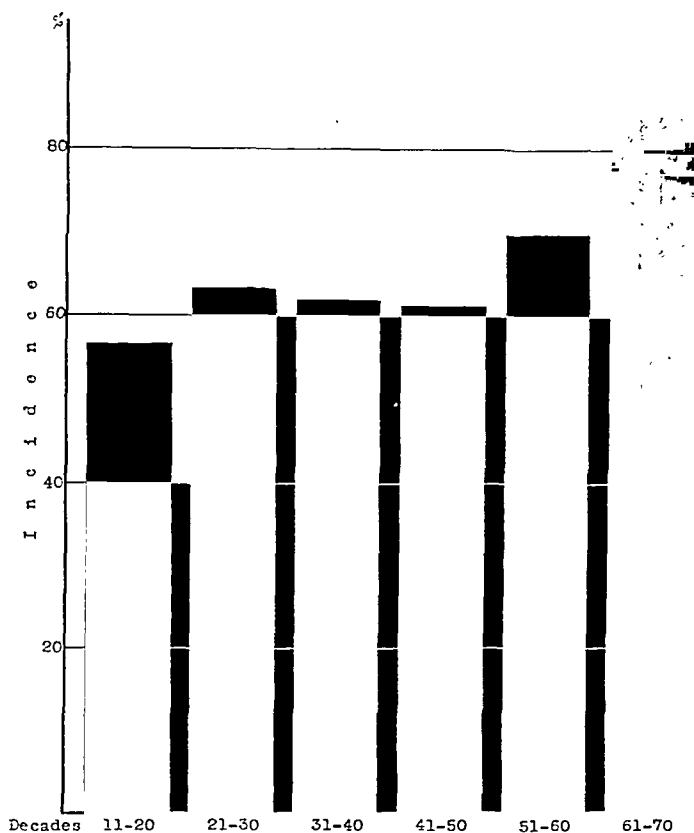


Chart 7.—Incidence of total appendices with inflammatory change according to age.

To summarize the effect of age on the incidence of inflammatory changes found in these appendices:

There was an increased incidence of inflammatory change with increasing age of the patients from whom the appendices were removed (charts 3 and 7). This increase in pathologic change was found slightly greater when the appendices which showed atrophic changes were added to those showing inflammatory change (chart 3).

The incidence of appendixes without inflammatory change (charts 3 and 4) and of the appendixes with chronic periappendicitis (chart 15) and acute periappendicitis (chart 16) decreased with increasing age.

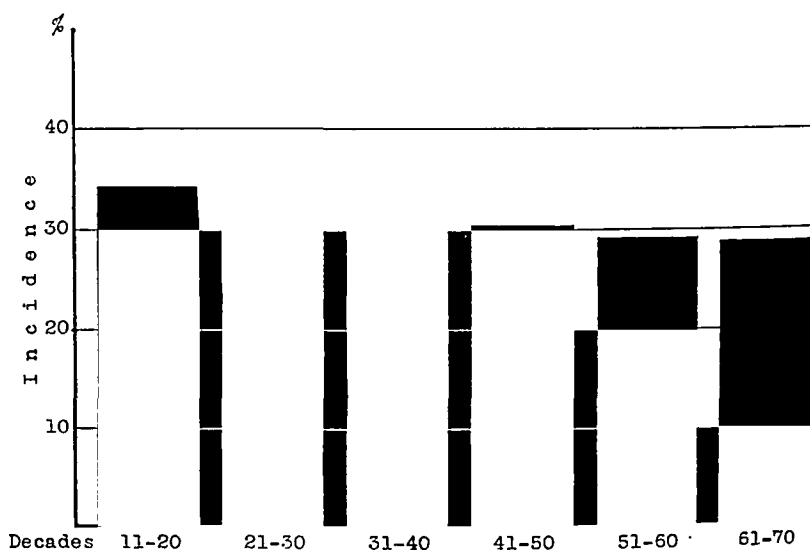


Chart 8.—Incidence of simple chronic appendicitis according to age.

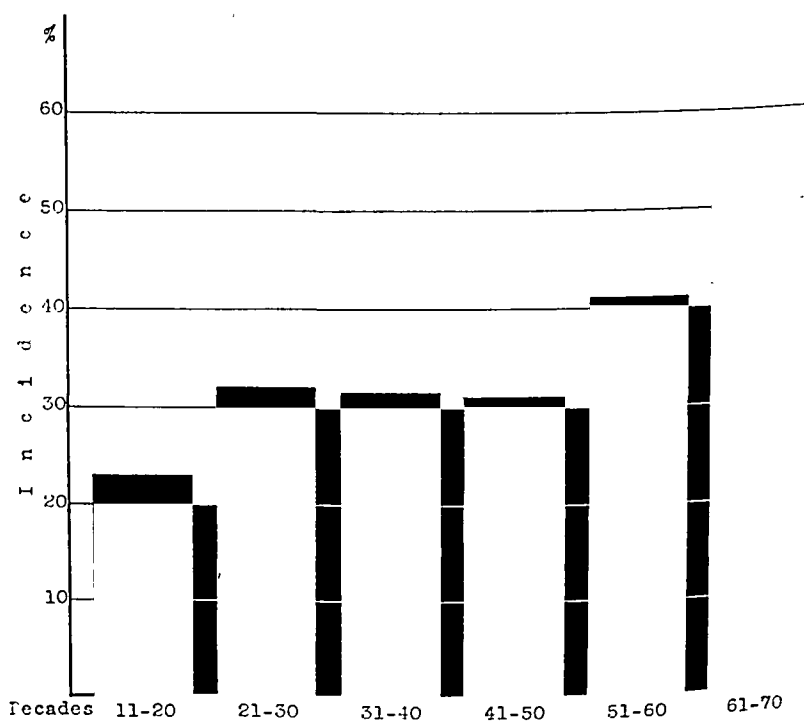


Chart 9.—Incidence of appendixes with marked inflammatory change according to age.

The incidence of chronic exudative appendicitis (chart 9) and acute appendicitis (chart 10) showed no increase with an increase in age.

TABLE 11.—Incidence of Inflammatory Change in the Appendix According to Age

Age by Decades	Condition In Appendix									
	No Inflammation	Normal	Atrophic	Inflammation	Simple Chronic Appendicitis	Marked Inflammatory Changes	Chronic Catarrhal Appendicitis	Chronic Exudative Appendicitis	Chronic Obliterative Appendicitis	
									With Infiltration	Without Infiltration
1 to 10.....	1	1	0	4	2	2	0	0	0	0
11 to 20.....	19	18	1	25	15	10	0	3	1	1
21 to 30.....	151	139	12	258	127	131	20	38	14	1
31 to 40.....	271	215	29	441	216	226	41	54	31	27
41 to 50.....	297	182	25	331	163	168	10	40	17	63
51 to 60.....	46	40	6	106	43	63	9	18	8	68
61 to 70.....	1	4	0	21	7	14	2	2	13	19
71 to 80.....	0	0	0	2	1	1	0	0	6	4
Totals.....	702	629	73	1,188	573	615	82	157	106	183
									33	31
										23
										1,800

TABLE 12.—Percentage Incidence of Various Types of Inflammatory Change in the Appendix According to Age *

Age by Decades	Condition In Appendix									
	Total Cases	No Inflammation	Atrophic	Inflammation	Simple Chronic Appendicitis	Marked Inflammatory Changes	Chronic Catarrhal Appendicitis	Chronic Exudative Appendicitis	Chronic Obliterative Appendicitis	
									With Infiltration	Without Infiltration
1 to 10.....	5	20.00	20.00	80.00	40.00	40.00	0.00	0.00	0.00	0.00
11 to 20.....	41	43.18	40.91	2.27	31.09	22.73	0.00	0.82	2.28	0.00
21 to 30.....	409	36.82	33.08	2.81	31.05	32.13	4.80	9.29	3.42	2.28
31 to 40.....	715	38.32	31.23	4.09	30.07	31.61	5.73	7.83	4.76	6.64
41 to 50.....	538	38.47	33.83	4.64	31.21	31.21	1.83	7.44	2.38	8.81
51 to 60.....	162	30.20	26.18	4.08	30.20	41.45	5.02	11.81	1.49	12.61
61 to 70.....	25	16.00	16.00	0.00	28.00	56.00	8.00	8.00	0.00	12.00
71 to 80.....	2	0.00	0.00	100.00	50.00	0.00	0.00	0.00	21.00	16.00
Totals.....	1,890	37.15	33.28	3.87	30.31	32.51	4.34	8.31	5.61	9.08
									1.75	1.61
										1.22

* The percentages were calculated on the total number of appendices in each decade. This table is shown graphically in charts 3 to 10.

The incidence of appendixes with inflammatory change (chart 7) and those with marked inflammatory change (chart 9) increased with age; there was also a similar increase in the incidence of chronic catarrhal

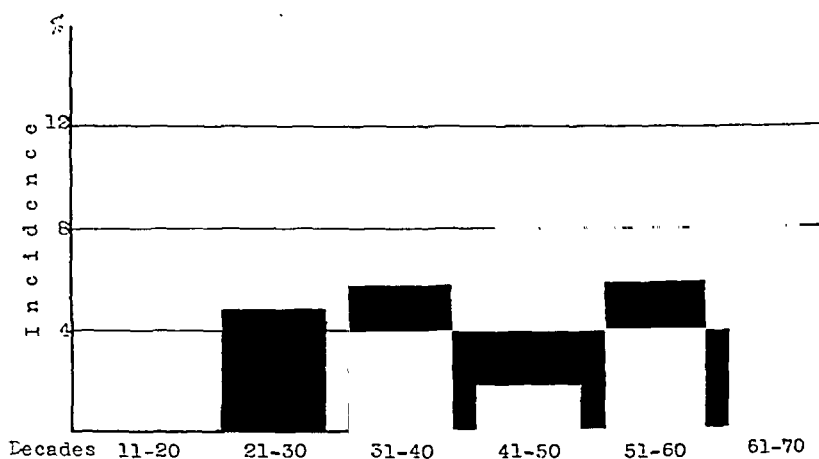


Chart 10.—Incidence of chronic catarrhal appendicitis according to age.

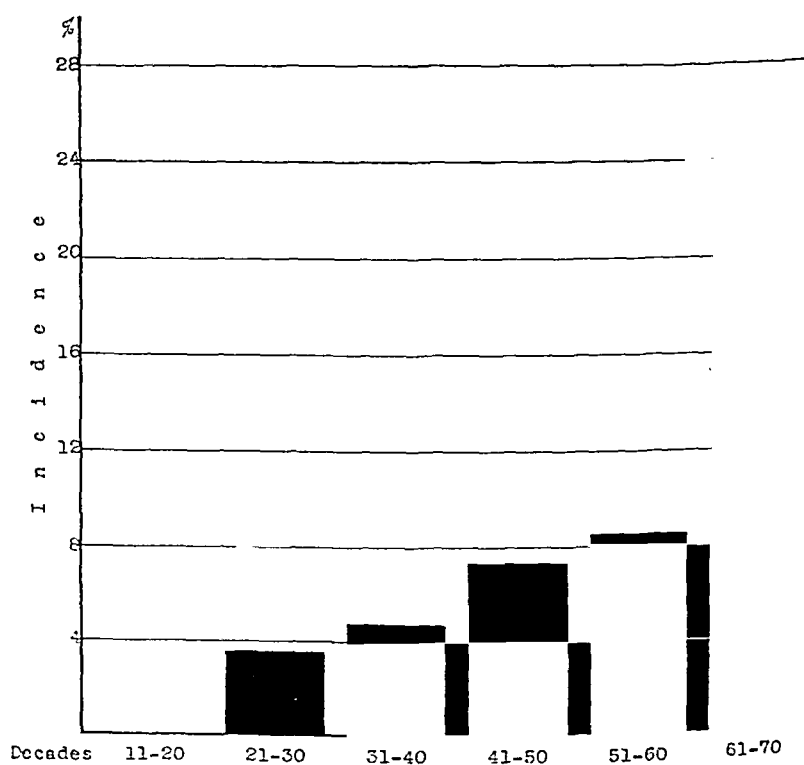


Chart 11.—Incidence of chronic obliterative appendicitis with infiltration according to age.

ral appendicitis (chart 10), atrophic appendicitis (chart 6), chronic obliterative appendicitis without infiltration (chart 12) and chronic obliterative appendicitis with infiltration (chart 11).

OTHER PATHOLOGIC CONDITIONS

Oxyuris in the Lumen of the Appendix.—Three appendixes were found to contain *Oxyuris* in the lumen, an incidence of 0.2 per cent. The pathologic conditions in these appendixes were classified as follows:

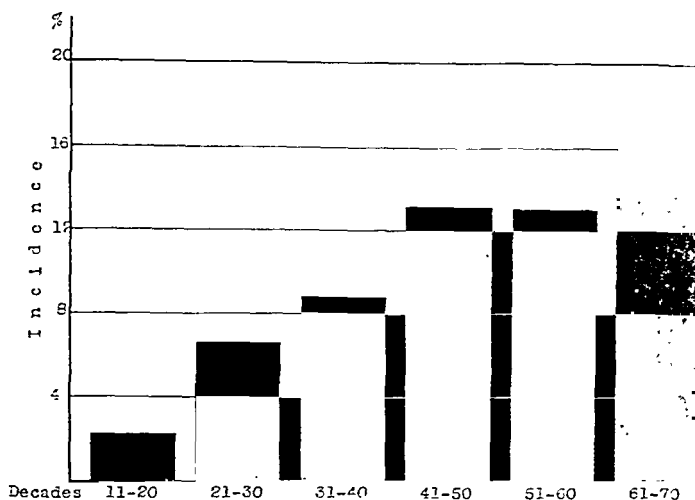


Chart 12.—Incidence of chronic obliterative appendicitis without infiltration according to age.

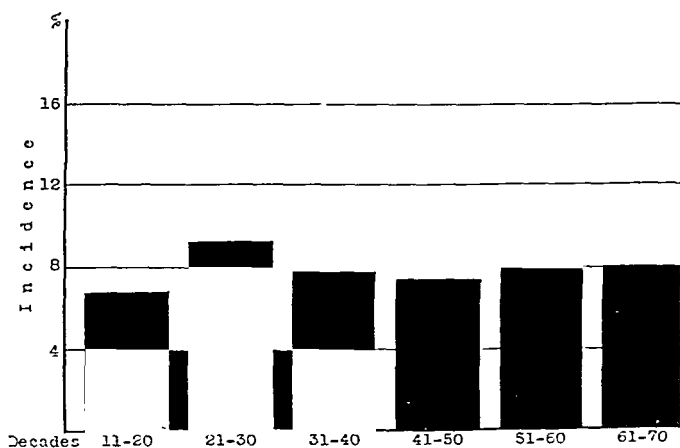


Chart 13.—Incidence of chronic exudative appendicitis according to age.

simple chronic appendicitis, chronic obliterative appendicitis with infiltration and acute catarrhal appendicitis. Two of the patients were operated on because of retroversion of the uterus and the other because of an ovarian cyst. Their ages were 30, 30 and 32 years.

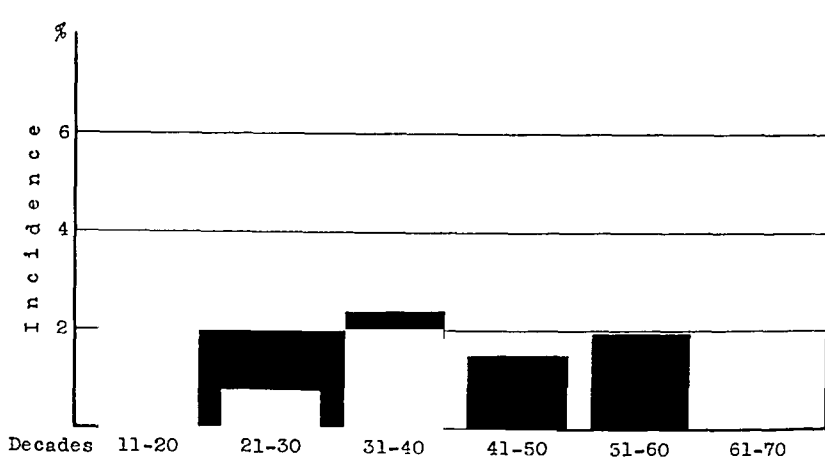


Chart 14.—Incidence of acute appendicitis according to age.

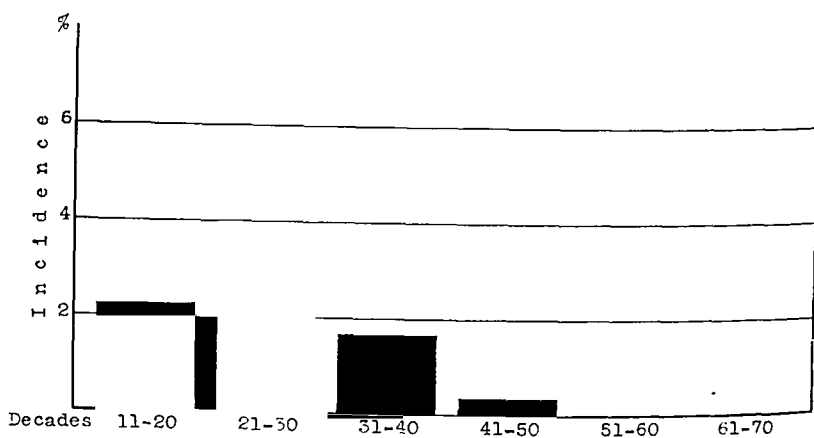


Chart 15.—Incidence of chronic periappendicitis according to age.

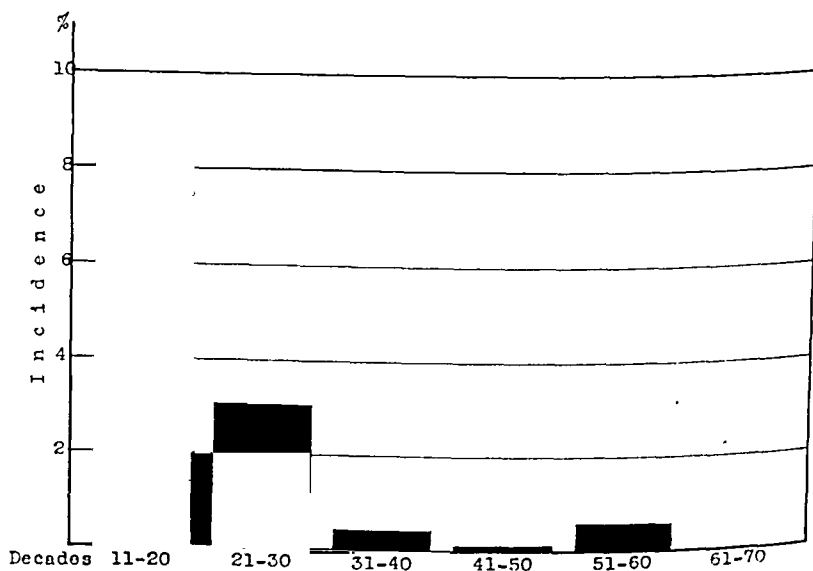


Chart 16.—Incidence of acute periappendicitis according to age.

Mucocele of the Appendix.—Mucoceles were found in 3 appendixes, an incidence of 0.2 per cent. One patient was operated on for intestinal obstruction due to adhesions and the other 2 for fibromyomata uteri. Their ages were 30, 44 and 75 years.

Tuberculosis of the Appendix.—This condition was found in 5 appendixes, an incidence of 0.3 per cent. Three appendixes showed chronic tuberculous appendicitis when no other tuberculous condition was noted in the abdomen. One was removed at the same time as the gallbladder, a diagnosis of chronic cholecystitis with cholelithiasis having been made. Another was removed at an operation for chronic salpingitis, but microscopic examination revealed no evidence of tuberculosis. The third was removed at the time of an operation for fibromyomata uteri.

TABLE 13.—*Pathologic Conditions Found in the Appendix, Other Than Inflammatory Change or Its Absence, With Incidence**

Pathologic Condition	Number of Cases	Incidence, Percentage	Number of Deaths	Mortality, Percentage
Oxyuris in the lumen.....	3	0.16	0	0.00
Mucocele.....	3	0.16	0	0.00
Tuberculosis.....	5	0.26	1	20.00
Diverticulum.....	1	0.05	0	0.00
Hyperplasia of the mucosa.....	3	0.16	0	0.00
Tumors.....	6	0.32	0	0.00
Totals.....	21	1.11	1	4.76

* The incidence was calculated on the basis of the 1,994 appendixes examined microscopically.

I repeat for emphasis that the histories and physical examinations in these 3 cases and in the following cases revealed no symptom or sign referable to the appendix.

The fourth appendix presented chronic tuberculous appendicitis in conjunction with a tuberculous cecum, the original operation having been done for fibromyomata uteri and retroversion.

The fifth appendix was removed from a patient who had acute tuberculous peritonitis. Microscopically it showed subacute tuberculous appendicitis. The patient died of generalized tuberculosis.

The age incidence in these cases was 20, 32, 35, 38 and 42 years.

Syphilis.—Microscopic evidence of syphilis was not found throughout the series, although a number of the patients had positive Wassermann reactions.

Diverticulum of the Appendix.—One appendix contained a diverticulum, an incidence of 0.1 per cent. The original cause for operation was ectopic endometrium on the pelvic peritoneum. The patient was 34 years old.

Hyperplasia of the Mucosa.—Three appendixes showed marked hyperplasia of the mucosa, an incidence of 0.2 per cent; in 1 instance it

was described as papillary and in the other as adenomatous. This condition follows an inflammatory process and cannot be classified as a new growth in this stage. Two of the primary operations were performed for fibromyomata uteri and 1 for a parovarian cyst. The ages of these patients were 26, 38 and 42 years.

Tumors of the Appendix (table 14).—Four appendixes showed endometrial rests, an incidence of 0.2 per cent. Three were from patients operated on for fibromyomata uteri and the other from a patient operated on for retroversion and chronic salpingitis. Their ages were 38, 42, 44 and 50 years.

A carcinoid of the appendix (an incidence of 0.1 per cent) was found in a patient 45 years old who was operated on for fibromyomata uteri.

One appendix contained a papillary adenoma, possibly malignant (an incidence of 0.1 per cent). The patient, aged 26, was operated on because of a tubal pregnancy.

TABLE 14.—*Types of Tumors Found in the Appendixes Studied, With Their Incidence**

Tumor	Number of Cases	Incidence, Percentage	Number of Deaths
Endometrial rests.....	4	0.21	0
Carcinoid.....	1	0.05	0
Papillary adenoma, possibly malignant.....	1	0.05	0

* This was calculated on the basis of the 1,904 examined microscopically.

It is of interest that none of the 1,904 appendixes examined microscopically showed a definite malignant process and that only 2 contained lesions which were questionably malignant.

SUMMARY AND CONCLUSIONS

Statistics on a group of 2,065 incidental appendectomies have been presented. These appendectomies were performed on patients whose histories and physical examinations gave no evidence of past or present appendical disease. The appendectomies included all those falling within the described definition which were done at St. Luke's Hospital (from both the private pavillion and the wards) in eleven years (1925 to 1935 inclusive). The pathologic conditions found in the 1,904 appendixes examined microscopically have been presented in the various tables and charts.

These findings may be stated briefly as follows: One third of the appendixes were either normal or relatively normal. Just less than one third showed slight to moderate, but definite, inflammation (simple chronic appendicitis). Over one third presented evidence of marked pathologic change. The latter group included those with types of appendicitis other than simple chronic appendicitis, together with atrophic

appendixes and those which showed other pathologic conditions, as listed in table 13.

Inflammatory changes are found in a considerable percentage of appendixes in the absence of a history or physical findings indicative of a pathologic condition in the right lower abdominal quadrant. In this series, 62 per cent fell within this class. More than half (51 per cent) of these showed marked inflammatory changes (32 per cent of the total number).

A slight but definite increase in inflammatory change in the appendix occurs in the presence of inflammation elsewhere in the abdomen. This becomes a marked increase with chronic suppurative and acute salpingitis and with peritonitis.

Acute appendicitis, even with actual suppuration, can exist without any subjective or objective evidence of its presence. The incidence was 1.7 per cent in this series.

A study of the cases in which the gallbladder was removed showed no increase in the incidence of cholecystitis in the presence of inflammation in the appendix. From this finding the statement can be made positively that no evidence is found to indicate that inflammation in the appendix causes inflammation in the gallbladder.

With increasing age there is a definite increase in the incidence of atrophic and inflammatory changes in the appendix. This is most marked with chronic obliterative appendicitis. It does not hold true for peri-appendicitis, which is caused by conditions prone to occur in early and early middle life.

The incidence of pathologic change other than inflammation is very low. This would indicate that these other conditions ordinarily produce symptoms referable to disease in the appendix.

When the appendix is not the cause of symptoms and there is no inflammation elsewhere in the abdomen, the expected incidence of pathologic change in the appendix is represented by the top row of figures in table 10. I shall refer to these figures in a study of the symptom complex attributed to chronic appendicitis.

Although the figures are not presented, I feel that it is worth while to mention the fact that the incidence of postoperative complications was found to be no greater than would be expected in a similar list of operations in which appendectomy was not performed. Also, no increase in mortality was found. From this the conclusion may be drawn that in properly selected cases, i. e., in those in which the nature of the operation and the patient's condition are favorable, the incidental removal of the appendix is a safe and worth while procedure.

The pathologic examination of all the appendixes listed in this paper was made by Dr. Leila C. Knox, pathologist at St. Luke's Hospital.

182 East Seventy-Ninth Street.

CHRONIC FUNCTIONAL LESIONS OF THE SHOULDER

A. W. MEYER, M.D.

STANFORD UNIVERSITY, CALIF.

It is difficult to find a title sufficiently noncommittal and inclusive and yet specific enough to designate the things I wish to consider. The word chronic in the title is used in a literal sense and entirely without any implication of disease, although some of the bony changes associated with these lesions simulate some of those commonly attributed to arthritis. I believe that the lesions here considered are not primarily or to any considerable degree due to the extraordinary uses to which the upper extremities are put but are caused merely by the ordinary, often repeated, everyday uses. They are hour to hour, day to day, month to month, year to year and decade to decade effects. It must not be overlooked, however, that some of the structures affected by function may be weakened gradually and eventually rupture under relatively slight strains, evoking symptoms out of all proportion to the forces involved at the time.

In considering the production of the lesions in question, one must divest oneself of the idea that the shoulder joint is a marvel of mechanical perfection. Even a cursory survey of its architecture should correct such a mistaken view. One may, I presume, grant that the human shoulder may be adapted perfectly to the uses for which it may have been intended, but certainly no one can rightly maintain that it is perfectly adapted for the uses to which it is put. These uses require a truly universal joint, and the humeroscapular articulation is such a one only imperfectly and only by subjecting the surrounding soft parts to repeated trauma. Even slight trauma recurring in the same place for hours, days, weeks and months has a cumulative effect and may produce great changes. It is hence no wonder that the reparative powers of the structures concerned often are exceeded and that repeated slight trauma may provoke an obliterative endarteritis and sclerosis. Moreover, since the individual trauma may fall below the threshold of reflex protective responses, there may be little to forestall the cumulative effect, and it is important to remember that it is the repetition and not the range of motion that counts.

Although I shall confine my remarks to the shoulder, I do not mean to imply that the functional lesions under consideration here occur nowhere else in the body. They are commonest and most pronounced

From the Department of Anatomy, Stanford University School of Medicine.

in the shoulder and also seem to occasion the greatest amount of discomfort and disability there. Some of them may occur anywhere else where motion is possible, no matter how slight the range, and they always become evident to the unaided eye after adequate repetition of the motion. However, I have seldom noticed them before the third decade of life. The average age of the bodies from which the specimens for the illustrations were taken was over 60 years.

LESIONS CONCERNED

The lesions vary greatly in their intensity and manifestations from joint to joint and person to person. Although abnormal or pathologic conditions may facilitate and also markedly accentuate them, I am deliberately excluding changes due to disease and am confining my attention to the effects of normal use alone. In the last analysis, of course, these lesions are traumatic, but they are not that in the customary meaning of that word. They undoubtedly are not accompanied by hemorrhage or some other phenomena associated with lesions ordinarily regarded as traumatic; yet the distinction is quantitative rather than qualitative. Among the lesions concerned are the following:

1. Fraying and partial destruction of the inner surface of the walls of the subdeltoid bursa and of the supra-acromial bursa, when present, and of the deeper bursae about the shoulder.

2. Fraying and partial or complete destruction of considerable portions of the articular capsule, both from within and from without, and of the coracohumeral and the inconstant superior and middle glenohumeral ligaments.

3. Fraying and partial or complete division or detachment of the tendon of the supraspinatus and partial destruction of that of the infraspinatus and of the long tendon of the biceps and that of the subscapularis.

4. Partial or complete erosion of the coraco-acromial ligament.

5. Perforation of the acromioclavicular articulation below and complete destruction of the deeper portion of the articular capsule.

6. Partial or complete dislocation of the pretubercular and the intertubercular portions of the long tendon of the biceps.

7. Thinning and complete local destruction of the articular cartilages, both hyaline and fibroid, in the humeroscapular and the acromioclavicular articulations.

8. Fraying of the under surface of the deltoid muscle and complete destruction of a large part of its middle portion.

9. Polishing and eburnation of the bony surfaces that come into movable contact after destruction of the overlying or intervening soft parts and cartilages.

10. Partial or total destruction of the articular fibrocartilage and of the articular disk and the cartilage on the clavicle and acromion; opening of the acromioclavicular joint from below with or without bony polishing, sometimes even in cases of ununited acromions.

11. Formation of a true coracoclavicular articulation with or without bony contact between the clavicle and the coracoid process and consequent polishing.

12. Polishing of the coracoid process from contact with the head and tuberosities of the humerus.

13. Considerable loss of bone from wear in the areas of bony contact.

CONDITION OF BURSAE

An anatomist seldom encounters smooth superficial synovial bursae in cadavers past middle age. Since the amount of fluid in a normal bursa is limited to mere moistening of its internal surface, normal bursae are not distended, and their walls hence are constantly in contact with each other except for a thin film of fluid. Were they lined by a layer of epithelium, endothelium or highly specialized mesothelium, such as that in the peritoneum, pleura and pericardium resting on a subserosa, one might expect the bounding membranes to become detached from the connective tissue on which they rest, but the absence of such a mesothelium and basement membrane and the existence of a gradual transition from the surface layer of flattened, stellate mesothelium to ordinary connective tissue make such a separation impossible. It follows from this that he who does a "synovectomy" really does not remove a membrane but merely destroys the innermost portion of the connective tissue of an articular capsule.

Instead of a smooth inner surface in synovial bursae, roughening and fraying and complete destruction of it are frequently encountered. Such conditions commonly exist in the subacromial and the supracapsular portion of the subdeltoid bursa and may be present in any or most of the thirteen or more bursae which may be associated with the humeroscapular articulation. It is mainly these portions of the surfaces of the subdeltoid bursa which are brought into firm contact with every abduction of the arm. Hence the rest of the roof and the floor of the bursa usually are intact and normal, even after the entire upper portion of the articular capsule has been destroyed and when bony polishing is present on the tuberosital portion of the humerus which comes into contact with the acromion. Whenever the subdeltoid bursa is large, it extends distally onto the shaft of the humerus beyond the tuberosities and under the coracoid process, but the walls of this portion may then also be wholly preserved. The areas of most intimate and frequent contact are always the first to show change, although it sometimes happens that one of three possible independent subcoracoid bursae may show complete destruction of its smooth inner surface, although the smooth surface of the two other contiguous bursae may be unaffected. It has often been asserted that roughening and destruction of the normal walls of bursae are the result of inflammation, or bursitis. While recognizing fully the changes that may be effected by chronic inflammation in bursae, the lesions here considered manifestly were not produced in that way, and it is well to emphasize that long-continued movement of soft parts on each other frequently effects roughening and fraying of the apposed structures. This, to be sure, applies also to articular cartilages, both hyaline and fibroid.

It is of great significance that similar effects of wear are met with also between structures which normally are not separated by bursae, such as the radius and the muscles and the tendons of the long abductor and the long and short extensor muscles of the thumb and the extensor carpi radialis longus muscle. Such an instance is represented in figure 1, a photograph of a specimen taken from a right forearm which showed no evidence of any pathologic condition or of injury, past or present. It will be recalled that loose connective tissue normally separates these structures in this region of the antibrachium. This tissue evidently was destroyed and the coapted surfaces of the muscles and tendons frayed by wear from often repeated rotation of the radius. This may have occurred under the pressure of a sling, a lever or a

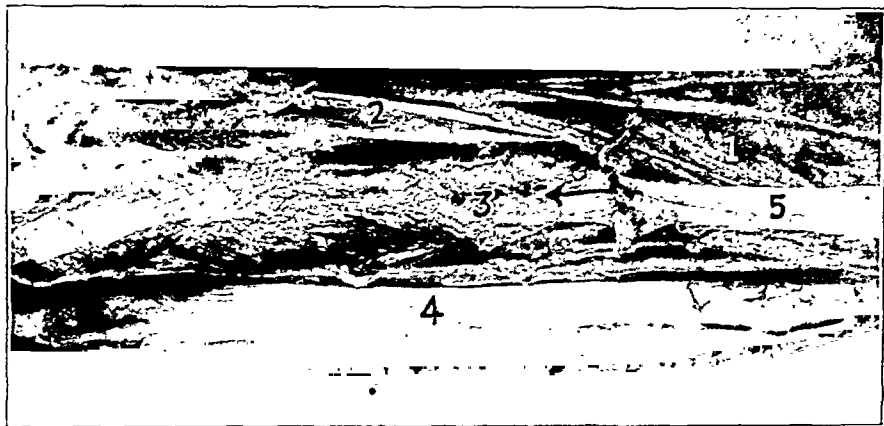


Fig. 1.—Fraying on the surfaces of the tendons and bellies of the abductor pollicis longus, the flexor pollicis longus, the extensor pollicis brevis and the extensor carpi radialis longus and of the loose connective tissue and the underlying periosteum in the left arm of a man 44 years of age. The tendon of the brachioradialis was reflected distally, and the photograph was taken from the side and in front with the forearm in semipronation. The belly of the abductor pollicis longus is indicated by 1, the deeper surface of the extensor carpi radialis longus and brevis by 2, the belly of the flexor pollicis longus by 3, the tendon of the flexor carpi radialis by 4, the tendon of the brachioradialis, reflected, by 5 and the tendon of the palmaris longus, on the edge, by 6. The arrow points to the most deeply worn portion of 3.

snugly fitting arm band, although probably none of these things are indispensable factors.

CAPSULAR DEFECTS

The forces which destroy synovial surfaces must of necessity produce similar effects on the underlying or deeper, outer bounding structures. Hence the articular capsule of the shoulder and the associated tendons may become similarly affected. The superficial surface of the

portion of the capsule immediately proximal to the greater tuberosity usually is the one to suffer roughening and fraying first, although roughening may also be evident on the inner surface of the capsule where it comes into contact with the margin of the articular cartilage. Thinning of the capsule and of the tendon of the supraspinatus muscle likewise usually occurs first proximal to the greater tuberosity, and perforation of the tendon and capsule usually is first seen here, as shown in figure 2. It may, however, also occur more ventrally or anteriorly to the tendon of the supraspinatus muscle in



Fig. 2.—Fraying of the inner surface of the subdeltoid bursa and an oval defect in the distal portion of the supraspinatus tendon with its long diameter in a longitudinal direction, indicated by the arrow.

the region under the coracoid process and even in the dorsal portion of the capsule, which is associated with the tendon of the infraspinatus muscle, as shown in figures 3 and 4 and represented by Meyer¹ in

1. Meyer, A. W.: Further Observations upon Use-Destruction in Joints, *J. Bone & Joint Surg.* **4**:491-511, 1922. See also: Meyer, A. W.: Anatomical Specimens of Unusual Clinical Interest, *Am. J. Orthop. Surg.* **13**:86-95, 1915; Further Evidence of Attrition in the Human Body, *Am. J. Anat.* **34**:241-267, 1924; Spontaneous Dislocation of the Tendon of the Long Head of the Biceps Brachii: Report of Four Cases, *Arch. Surg.* **13**:109-119 (July) 1926; The Minuter Anatomy of Attrition Lesions, *J. Bone & Joint Surg.* **13**:341-360, 1931.



Fig. 3.—Right shoulder viewed from above, showing defects in the articular capsule anterior and posterior to the unruptured tendon of the supraspinatus. The dorsal defect is indicated by 1, the long tendon of the biceps lying in a large ventral defect, by 2, the coraco-acromial ligament by 3 and the clavicle by 4.



Fig. 4.—Two large attrition defects (1 and 2) in the dorsal portion of the capsule of the shoulder. The tendons of the infraspinatus and teres minor were practically intact. The cartilaginous margin of the head of the humerus responsible for these defects can be seen clearly across the lower defect, forming a slightly irregular border below 2. The two defects are separated by a narrow strip of capsule on either side of which the (white) articular cartilage of the head of the humerus can be seen.

figures 8 and 9. The latter defects always are produced from within but the former largely from without, and they may be present when all the other articular structures are practically normal. Whenever the margin of the acromion or its under surface is rough or studded with small periosteal osteophytes, the superficial layer of the capsule, the tendon of the supraspinatus muscle and the deeper, thicker portion of the capsule, which may all be detached from each other, forming separate layers, may show parallel longitudinal scoring or ribboning, as shown in figures 5 and 6.

In cases of maximal capsular destruction, the entire upper portion is absent, the tendon of the infraspinatus muscle is forced backward and downward and that of the subscapularis muscle may be detached completely from the lesser tuberosity, maintaining its attachment to the adjacent diaphysis only. However, one can always find the retracted, more proximal, portion of the capsule under the acromion, for although retracted and sometimes somewhat folded, it always presents a thin, sclerotic, falciform border.

It is of much moment in connection with the causation of capsular defects into the shoulder joint from above that they may occur on either side of an unruptured and intact tendon of the supraspinatus muscle. Sometimes they are present on both sides of this tendon and may be represented by mere longitudinal slits, such as those represented at 2 and 3 in figure 7 and in figure 8. The character and direction of these defects show that they could not have been produced by pull of the muscle or rupture of a tendon, least of all by rupture of that of the supraspinatus, and the entire absence of evidence of disease in these cases shows that it cannot have been a factor in their production.

Whenever the periosteum distal to the capsular and tendinous attachment on the greater tuberosity of the humerus and that under the acromion are destroyed through contact, polishing and eburnation of the underlying bone are inevitable if adequate motion continues. Since the periosteum possesses marked osteogenetic powers, small osteophytes or exostoses not infrequently develop in the areas undergoing denudation if the necessary conditions prevail. This is what one should expect, and whenever osseous roughening occurs on the distal margin or the under surface of the acromion, the destruction of the superficial layer of the joint capsule is greatly facilitated and so is that of the tendon of the supraspinatus and the deeper, thicker portion of the capsule and of the capitular articular cartilage when it comes into contact with the acromion. This does not imply, however, that the articular cartilage on the head of the humerus may not be worn away elsewhere, for this frequently is the case.

After destruction of the upper portion of the articular capsule and its included tendons, the deeper surface of the deltoid muscle will be

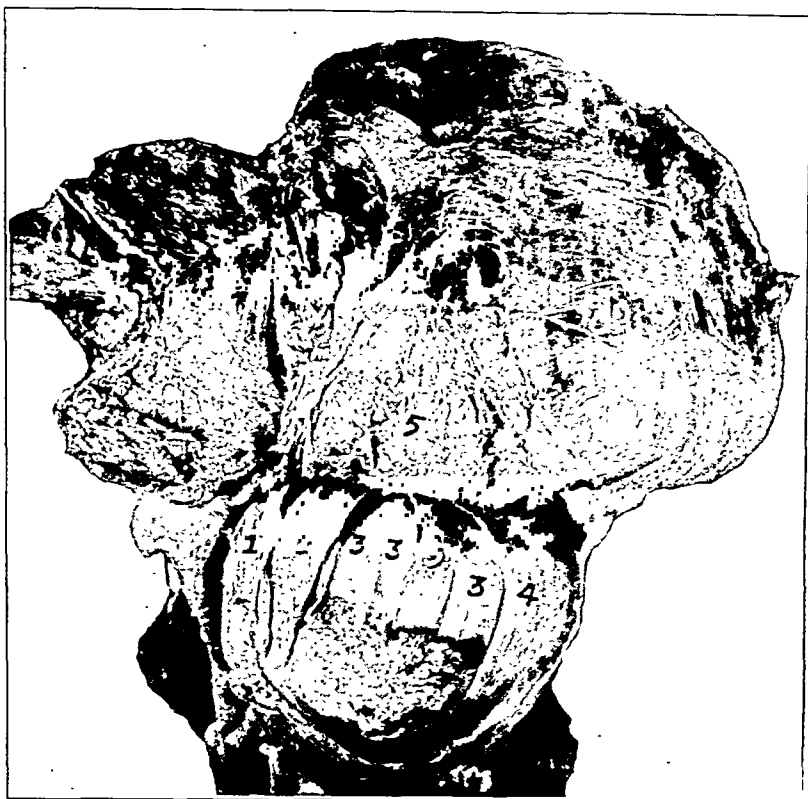


Fig. 5.—Right shoulder with the deltoid reflected upward, revealing a large oval defect in the tendon of the supraspinatus bordered by smooth, sharp-edged margins of the latter (2) and (4), below which lie longitudinal ribbons of the deeper portion of the articular capsule (3). A frayed superficial part of the capsule is indicated by 1, and the frayed deltoid portion of the subdeltoid bursa, by 5. Not all longitudinal trabeculae of the capsule were numbered; a very narrow one lies between 1 and 2.



Fig. 6.—A left shoulder joint with a similarly frayed and trabeculated capsule and tendon of the supraspinatus. It should be noted that all the trabeculae are longitudinal in direction with respect to the tendon of the supraspinatus.

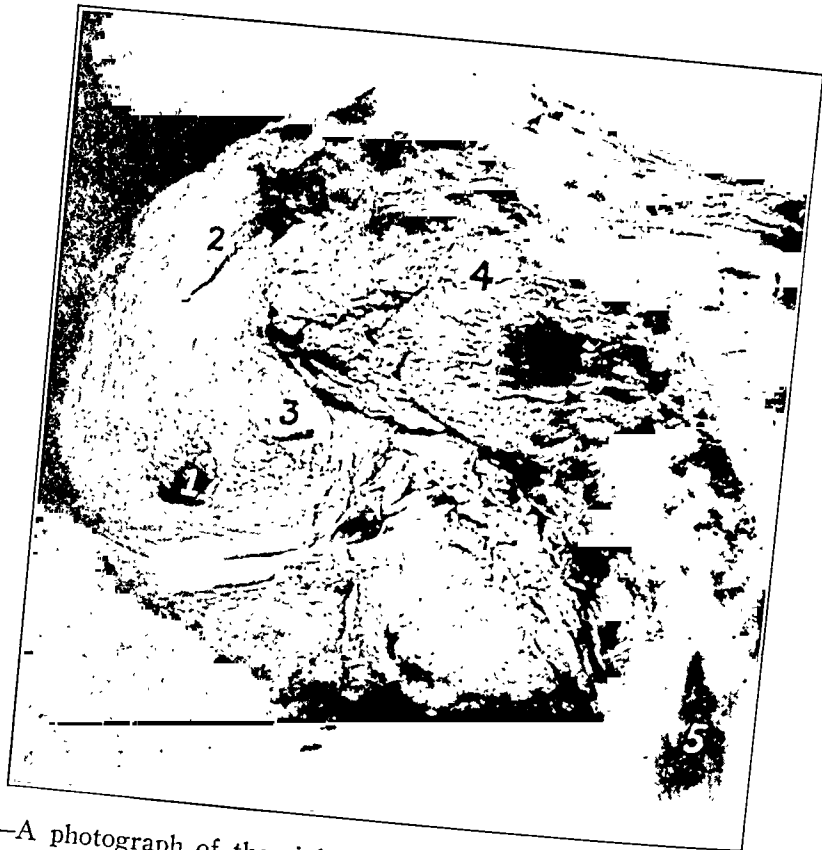


Fig. 7.—A photograph of the right shoulder from in front and above. Longitudinal slits are seen at 2 and 3 on either side of an unaffected tendon of the supraspinatus. A large, irregularly shaped hole is seen at 1. The acromion is indicated by 4 and the clavicle by 5.

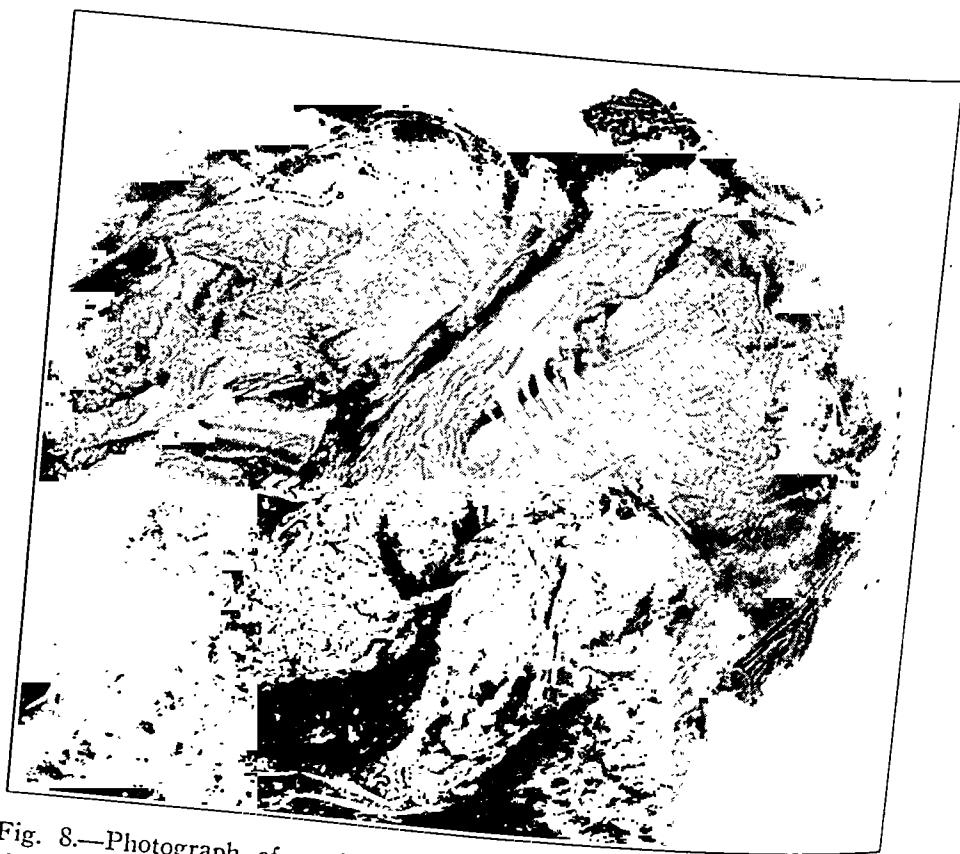


Fig. 8.—Photograph of a right shoulder in a similar view showing a long longitudinal slit at the smooth anterior border of an unaffected supraspinatus tendon. Fine, narrow trabeculae, remnants of the superficial layer of the articular capsule, are seen bridging the slit.

exposed to similar wear, for under such conditions it must act vicariously for the destroyed portion of the capsule. A large part of the midsection of the proximal portion of the deltoid muscle may be destroyed completely. Whenever this happens, only the skin, the subcutaneous tissues, the superficial and deep fasciae and the fused sheaths of the deltoid muscle remain as a cover for the joint, and it would seem that it should be possible to diagnose such a condition in life. Such extensive destruction must be relatively rare, however, for I have seen but a single example in about a thousand bodies and have learned of no other instance, although fraying of a portion of the under surface of the deltoid muscle is not uncommon.

CHANGES IN THE LONG TENDON OF THE BICEPS

It is interesting that the intra-articular portion of the long tendon of the biceps muscle may be destroyed completely without destruction of the articular capsule and without the presence of pathologic changes anywhere in or about the joint. The tendon usually shows wear from beneath, but evidences of this not infrequently are present also on its upper surface. Erosion along the lateral margins may be due to a disproportion in width between the more proximal, intra-articular, portion of the tendon, which often is much wider, and the lateral walls of the bicipital sulcus, although it is more commonly due to contact with slight irregularities on the walls of the sulcus, apparently the result of periosteal injury from wear. Fraying of the under surface of the tendon usually results from contact with the cartilaginous margin of the head of the humerus, with the supratubercular ridge (see fig. 3, Meyer²), when present, or with slight irregularities on the floor of the sulcus, representing reactions to wear, or from contact with the lesser tuberosity in cases of partial or total dislocation. Whenever the relatively rough surface of the lesser tuberosity comes into contact with this tendon after partial or total forward dislocation of it and detachment of the capsular attachment between the lesser tuberosity and the sulcus, destruction of the tendon is greatly facilitated, but whenever it remains in a capsular sling it may become completely dislocated without grossly evident wear.

It is surprising and also very significant that the tendon of the supraspinatus and the long tendon may reach paper thinness without rupturing. Indeed, it is not at all uncommon to encounter long tendons of which so small a fasciculus remains that it cannot bear a weight of 10 pounds.³ Yet I have never seen a case of acute rupture in the dis-

2. Meyer, A. W.: Spontaneous Dislocation and Destruction of Tendon of the Long Head of Biceps Brachii; Fifty-Nine Instances, *Arch. Surg.* **17**:493-506 (Sept.) 1928.

3. This no doubt is accounted for by the fact that secondary attachments are formed before the tendon is completely divided.

secting room, and I have never been able to find more than a proximal trace of the relatively long intra-articular portion of this tendon. This probably is due to division of it long before death and to destruction of the proximal portion by attrition and lysis.

An excellent specimen showing wear on both surfaces of the long tendon is represented in figure 9, which is a photograph of the intra-articular portion from the right shoulder of a man whose left tendon was wholly unaffected. The wear on the superficial or upper surface and on the anterior margin of this long tendon was due to contact with the overlying capsule—the so-called transverse humeral ligament.⁴ Wear

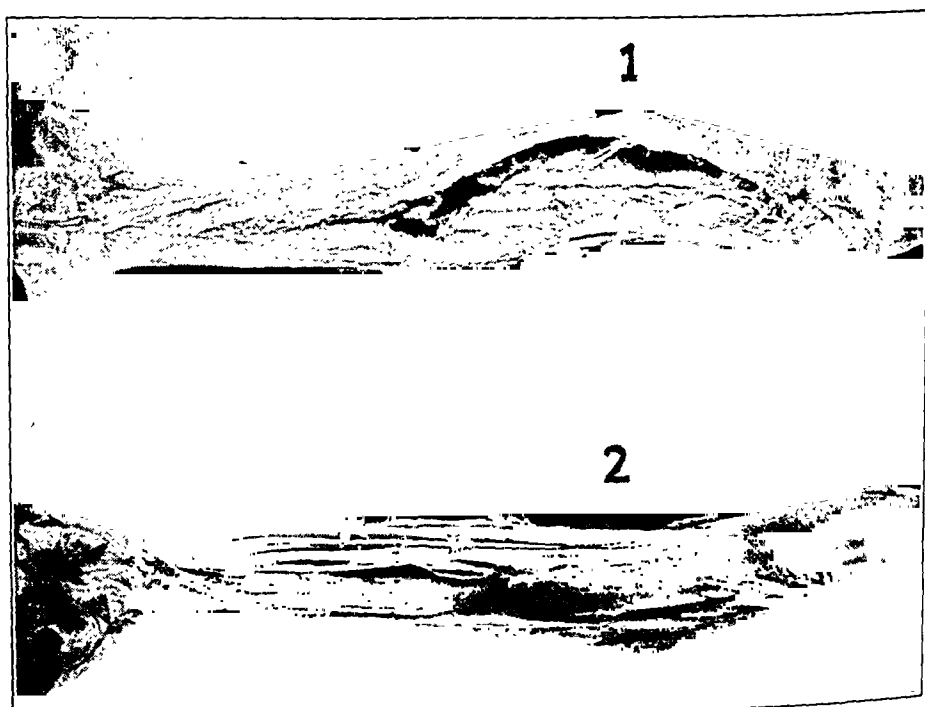


Fig. 9.—Right long tendon taken from a joint showing no evidences of disease. Both surfaces are markedly, though superficially, frayed. The proximal ends are to the left. Note the longitudinal fasciculation of the tendon, the detached synovial sheath and the fraying on both surfaces and the anterior margin to near the supraglenoid attachment.

on its under surface was from contact with a supratubercular ridge in the region of the lesser tuberosity. Since this tendon was undergoing spontaneous dislocation, its anterior margin and its upper surface were forced against the overlying capsular attachment, its dislocation being facilitated by the presence of a supratubercular ridge, which forced it

4. In cases of destruction of the overlying capsule, the superficial surface of the long tendon may also be worn by contact with the deep surface of the coraco-acromial ligament.

upward from the sulcus as well as forward. Under these circumstances, the tendon has to act as a wedge during its dislocation forward from the groove.

Whenever a portion of a tendon is deprived of the protective effect of the covering articular capsule and of its own sheath, its nutrition must of necessity be interfered with very seriously. At any rate, the portions of tendons so denuded become separated into longitudinal fasciculi of varying caliber. These readily become divided by contact with the cartilaginous margin of the head of the humerus or other surfaces of contact and may then easily be mistaken for portions of the tendon which were ruptured. This fasciculation of tendons is especially common on the under surface of the tendon of the subscapularis and of the tendons of the supraspinatus and the infraspinatus, but it occurs also on the upper or superficial portion of the tendon of the subscapularis and especially on the under surface of the long tendon of the biceps. I have encountered it in many places, even where the tendon of the peroneus longus glides on the facet of the cuboid bone, as shown in figure 10.

CHANGES IN THE TENDON OF THE SUPRASPINATUS

Fraying, thinning and final destruction of a part or the whole of the width and the thickness of the distal portion of the tendon of the supraspinatus as a rule are effected largely or wholly from without or above, while the tendons of the long head of the biceps and the tendons of the subscapularis and the infraspinatus usually are involved from within or beneath. However, the superficial portion of the tendon of the subscapularis may become fasciculated from movement against the under surface of a partially or wholly dislocated tendon of the biceps, after the protecting and overlying portion of the articular capsule has been detached or stretched to form a sling. Hence both surfaces of this tendon, like those of the biceps and of the supraspinatus, may suffer simultaneously, even if not equally.

Dislocation medially (forward) of the long tendon of the biceps may take place without detachment of the adjacent portion of the articular capsule, for the latter may merely stretch and form a sling which can glide on the long tendon in movements of the arm and protect it from contact with the underlying cartilage or bone. If the tendon of the subscapularis likewise retains its attachment, the long tendon may hence become dislocated completely without suffering much wear. But just as soon as the articular capsule becomes detached medially (anteriorly) and capitularly to the lesser tuberosity, dislocation of the intra-articular portion of the long tendon can begin; and it not infrequently becomes complete, although still in its normal position in the rest of the bicipital sulcus. Whenever the roof of the

intertubercular portion of the sulcus yields, the long tendon can gradually become dislocated forward over the lesser tuberosity and lie on the tendon of the subscapularis or on the lesser tuberosity itself, in case of detachment of the latter tendon from it. In the cases of the most maximal dislocation of the long tendon which I have seen, the more distal portion always lay in its normal position. This it does not leave either laterally or medially because of the firm attachment of the great tendons on either side and because of the directions of pull.

CHANGES IN CARTILAGES

The central area of the articular cartilage of the head of the humerus not infrequently also shows the effect of wear, but this does not imply that the central portion of the cartilage on the glenoid cavity must show the same effect, for a small portion of it is composed of fibroid instead of hyaline cartilage. The hyaline cartilage on the head of the humerus

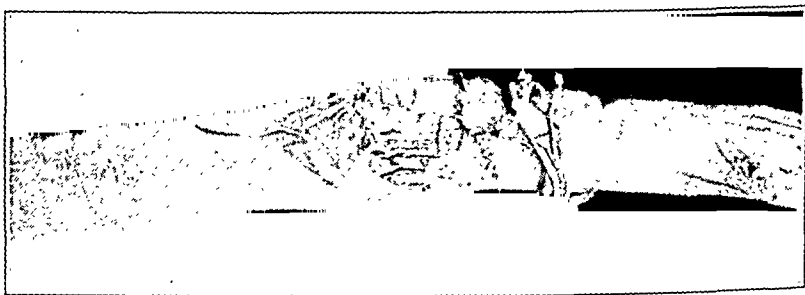


Fig. 10.—Right peroneus longus tendon seen from below with the distal extremity to the right. Note the detached synovial sheath near both extremities of the worn portion and the depth of the wear. The facet on the cuboid bone with which this worn area was in contact was normal in all respects and so were the rest of this tendon and its synovial sheath.

just proximal to the greater tuberosity may also be affected whenever it comes into direct contact with the under surface of the acromion, and it is in this region of the greater tuberosity and on the under surface of the acromion that polishing and eburnation are generally observed first. These polished areas seldom are congruent, however, and that is what one should expect. One may be several square centimeters in area, while the other coapted with it may be so small as to be scarcely noticeable, just as one can deface a large area with a fine diamond point.

The superficial membranoid layer of hyaline articular cartilage, which the older anatomists mistook for synovial membrane and which occasionally still is regarded so today, becomes frayed first. However, the thicker, uncalcified underlying layer not infrequently is chipped off from the underlying calcified layer in considerable areas over the head of the

humerus. Whenever the latter becomes detached, the underlying compacta is exposed, and polishing and eburnation can begin as soon as this area comes into contact with a similarly denuded area on the scapula or with an ossific plaque or nodule in the articular capsule. I have seen a number of such ossifications a centimeter or more in size which were exquisitely polished from contact with the head or the tuberosities of the humerus. Such nodules may also be polished on the external surface whenever they are in an area of the capsule which will permit them to come into contact with the acromion or the coracoid process.

Quite frequently the inferior acromioclavicular ligament and the respective portion of the capsule contain defects varying from small gaps to complete destruction of this portion of the capsule. Since shoulders with such defects which happened to come to my attention first also contained large defects in the upper portions of the humero-scapular articulations with complete division of the tendons of the supraspinatus muscle and partial destruction of the acromioclavicular ligaments, I had concluded that these defects in the acromioclavicular capsules and ligaments were due to contact with the heads of the humeri and the adjacent regions of the greater tuberosities. Of late I have observed a number of defects which cannot be accounted for in this way, however. In the latter instances the defects in the acromioclavicular capsule had been produced from above by contact with the inferior surface of the distal extremity of the clavicle and perhaps to some degree also by contact with the similar margin of the articular facet of the acromion. The lesion is surprisingly common and may be accompanied, preceded or followed, by the formation of a synovial bursa below this articulation in the connective tissue and fat overlying this portion of the supraspinatus muscle. Sometimes the musculotendinous junction is extensively fasciculated and frayed for an extent of several centimeters. Examples of these lesions with illustrations can be found in a forthcoming article on "Use Destruction in the Human Body," in *California and Western Medicine*.

Although in the long course of the gradual production of such lesions as these, slight hemorrhage may occur whenever a weakened structure suddenly yields, I have never encountered evidences of it. Thickened bursal walls and some coagulum were discovered only a few times in almost a thousand bodies, and effusions and adhesions were never seen. Gross and microscopic examination of a considerable series of specimens yielded no evidence of the presence of chronic inflammation.

Short distal stumps of the tendon of the supraspinatus muscle and of the adjacent capsule and transverse rents in the latter were seen only a few times. The defects and the fasciculations usually extended in the direction of pull, and the earliest capsular and tendinous defects

always were bounded by smooth, attenuated borders of capsule and tendon instead of by frazzled, thickened borders. Since, as shown in figures 7 and 8, longitudinal capsular defects also occur in the ventral (anterior) intertendinous portion of the capsule and broader defects also dorsally (posteriorly) beneath wholly uninjured tendons of infraspinatus muscles, these defects manifestly cannot be due to the rupture of associated tendons. The same thing is true of the fraying on the internal surface of the capsule opposite the cartilaginous margin of the head of the humerus and on the inner margin of the glenoid fibrocartilage, where fraying is practically universal. Rarely these cartilages may be nearly or wholly destroyed for a part of their extent.

The occasional presence of ossific nodules in different places in the upper half of the joint capsule, in the tendon of the infraspinatus muscle and even in the coraco-acromial ligament suggests that sudden trauma, greater in intensity than that which can be attributed to wear, may have been responsible for their production. That can readily be granted, for what laborer could be so fortunate as to escape sudden trauma to the shoulder during decades of an active life? The frank recognition of this fact surely cannot negate the overwhelming evidence against the assumption that all the lesions here considered result in this way or are the product of disease.

RUPTURE OF THE TENDON OF THE SUPRASPINATUS

Although Codman⁵ (p. 120) thought weakness of the tendon of the supraspinatus muscle is due to its evolutionary history and spoke (p. 144) of "the strain on this little tendon," he nevertheless said (p. 150) that the insertion of this tendon is $\frac{3}{4}$ inch (1.9 cm.) long. On the basis of the best calculations available, the more prevalent form of tendon of the supraspinatus has a tensile strength many times that of its muscle belly. According to Triepel,⁶ Fick,⁷ Cronkite⁸ and investigators mentioned by them, a supraspinatus tendon $\frac{3}{4}$ inch (1.9 cm.) wide and only 2 mm. thick could bear an estimated pull of over 700 pounds (318 Kg.), and one 3 mm. thick could bear a pull of over 1,000 pounds (454 Kg.). The muscle belly of the supraspinatus, on the other hand, even when it is large, has an estimated maximum

5. Codman, E. A.: *The Shoulder: Rupture of the Supraspinatus Tendon and Other Lesions in or about the Subacromial Bursa*, Boston, The Author, 1934.

6. Triepel, Hermann: *Einführung in die physikalische Anatomie*, Wiesbaden, J. F. Bergmann, 1902-1908.

7. Fick, Rudolf: *Handbuch der Anatomie und Mechanik der Gelenke unter Berücksichtigung der bewegenden Muskeln*, Jena, G. Fischer, 1910-1911, nos. 2 and 3; in von Bardeleben, K. H.: *Die Anatomie des Menschen*, Leipzig, B. G. Teubner, 1908, vol. 2, nos. 1 and 2.

8. Cronkite, Alfred Eugene: *The Tensile Strength of Human Tendons*, *Anat. Rec.* 64:173-186, 1936.

strength of only 170.9 pounds (77 Kg.). Since the tendon of the supraspinatus muscle with the included capsule often is considerably thicker than 3 mm., the true disproportion between the strength of the unworn tendon and that of the muscle is greater than the foregoing estimates indicate. This alone makes rupture of a sound normal tendon by active muscle pull alone doubtful, and even if such a relationship did not exist and the tendon were relatively too weak and then were torn in part only, thus reducing its ability to withstand the next maximal muscular contraction, it then should yield suddenly. Moreover, since the worn supraspinatus tendon always becomes gradually thinner toward the point of its insertion, where it may be of membranoid thinness without perforation, it follows that all such tendons should have yielded earlier to sudden muscle pull and that they should contain transverse instead of longitudinal tears and trabeculae. And how could one entertain the belief that contraction of the subscapularis can avulse the large tubercular portion of the tendon, always leaving the relatively small diaphysial attachment intact, or that the greater upper part of the insertion of the infraspinatus may likewise be detached and the small, weaker, lower portion always remain unruptured? Yet this was always the case in my observations. Sudden rupture of the sound supraspinatus tendon should leave normally thick or thicker ragged, blunt ends, and sudden detachment of the tendon from its insertion should leave the fractured or intact border of the greater tuberosity protruding to impinge suddenly against the acromion in abduction of the arm. Since the cervical sulcus of the humerus sometimes is deep here and the tuberosity very prominent, such a sequence of events certainly would make itself felt severely during life and would not escape the attention of the clinician. Gradual erosion of the tendon, on the other hand, whether from within or from without, gives atrophy an opportunity to produce its leveling and reducing effects, lowering the height of the greater tuberosity and thus rounding the contour of this region of the humerus. Any one sufficiently familiar with the changes in it and in the region of the lesser tuberosity is aware of the great reduction sometimes suffered, especially by the latter, after detachment of the tendon. The entire place of the lesser tuberosity sometimes is occupied by a smooth, sunken field and at other times by a somewhat rougher field than normal. Examination of the spongiosa beneath may reveal a large absorption cavity akin to Ward's triangle in the spongiosa of senile femurs (see fig. 1, Meyer⁹). I have never noticed equally marked atrophy of the spongiosa in the region of the greater tuberosity, but this may be due to the fact that since the latter continues to impinge

9. Meyer, A. W.: Unrecognized Occupational Destruction of the Tendon of the Long Head of the Biceps Brachii, *Arch. Surg.* 2:130-144 (Jan.) 1921.

against the under surface of the acromion, the underlying spongiosa is continually subjected to strains sufficient to preserve it from the marked atrophy of disuse to which that underlying the lesser tuberosity is subjected after detachment of the tendon of the subscapularis.

THE QUESTION OF ATROPHY

I am aware of the fact that atrophy of the supraspinatus muscle has been emphasized as a diagnostic sign of rupture of its tendon, but I have been able to detect the presence of marked atrophy of it only a few times in cadavers. This applies likewise to the lateral belly of the biceps and to that of the subscapularis and of the infraspinatus. It appears to me that the absence of marked muscular atrophy, even in the presence of pronounced lesions in the tendons of these muscles, may be accounted for by the fact that the tendons are divided gradually, that the nerve supply of the muscles is left intact and that they hence can respond and continue to contract against some resistance. Moreover, it must not be overlooked that the long tendon of the biceps gradually obtains a secondary attachment in the region distal to the tuberosities, usually the lesser tuberosity, and that those of the subscapularis and infraspinatus never become wholly detached. The invariable presence of such a secondary attachment of the biceps, it seems to me, is adequate evidence that sudden rupture probably did not play a part in these cases, for were this so, considerable elongation of the brachial portion of the tendon should be common instead of very rare. Moreover, the invariable reattachment of this tendon at the same level on the humerus could not be accounted for. Reports of cases of acute rupture in which operative treatment was employed (Gilcreest¹⁰) confirm these conclusions. On the other hand, since the tendon must yield gradually when weakened by wear, it obtains a secondary attachment before it is completely divided.

I have never seen any evidences of the existence of osteitis in the region of the lesser tuberosity, as described by Béra,¹¹ and do not believe that it could be a factor in reducing the size of the lesser tuberosity and thus facilitate dislocation of the long tendon of the biceps. Chronic osteitis, unless suppurative, should not cause destruction of the

10. Gilcreest, Edgar Lorrington: (a) Rupture of Muscles and Tendons, Particularly Subcutaneous Rupture of the Biceps Flexor Cubiti, *J. A. M. A.* **84**:1819-1822 (June 13) 1925; (b) Two Cases of Spontaneous Rupture of the Long Head of the Biceps Flexor Cubiti, *S. Clin. North America* **6**:547-554, 1926; (c) Dislocation and Elongation of the Long Head of the Biceps Brachii: An Analysis of Six Cases, *Tr. West. S. A.* **44**:260-296, 1934.

11. Béra, Albert: Du syndrome commun à la rupture, à la luxation et à l'élongation du tendon du long biceps, *Thèse de Paris*, no. 304, Paris, Jouve & Cie, 1911.

bone, and as long as the ligamentous, capsular and tendinous attachments remain intact, dislocation of the long head is impossible. The following words from Béra's splendid thesis deserve repetition, however:

Les anomalies congénitales.—Il est intéressant de faire remarquer que les anatomistes ont fréquemment cité des cas où la longue portion du biceps se fixait anormalement dans la coulisse bicipitale, sur les tubérosités humérales, sur la capsule de l'articulation de l'épaule (Dr. Le Double, *Variations du système musculaire de l'homme*, t. II). Il est permis de se demander si certains de ces faits ne rentrent pas dans le cadre de l'affection qui nous occupe; et si cette anomalie d'insertion n'est pas souvent l'effet secondaire d'un traumatisme plutôt que le résultat d'une malformation congénitale.—Ici encore, la perceptibilité du tendon bicipital au-dessous du bord deltoïdien, constatée sur le vivant ou sur le cadavre, permettrait de trancher la question [p. 48].

Cette luxation primitive et isolée existe-t-elle en tant qu'affection franche et persistante, la chose est peu probable. Elle entraîne non seulement l'ouverture de la coulisse bicipitale, mais encore la destruction de la capsule articulaire et du tendon du sus-épineux [p. 38].

Congenital Anomalies.—It is interesting to note that anatomists have frequently cited cases in which the long head of the biceps muscle was abnormally fixed in the bicipital groove, on the humeral tuberosities or on the capsule of the joint of the shoulder (Dr. Le Double: *Variations du système musculaire de l'homme*, vol. 2). It is allowable to ask whether some of these facts do not enter into the picture of the disturbance of which we treat and whether this anomaly of insertion is not often the secondary effect of a traumatism rather than the result of a congenital malformation. Perception of the bicipital tendon below the deltoid border in the living subject or in the cadaver would allow one to decide the question [p. 48].

That this primary and isolated luxation exists as a frank and persistent disturbance is improbable. It leads to not only the opening of the bicipital groove but also the destruction of the joint capsule and of the tendon of the supraspinatus muscle [p. 38].—Publisher's translation.

I have never seen a case of spontaneous dislocation of the long tendon dorsally over the greater tuberosity, and it seems to me that this is wholly precluded by normal anatomic conditions. All dislocations of the biceps tendon seen by me were forward dislocations, and I never saw any evidences that fractures or previous dislocations had been contributory factors in producing the lesions I am considering. However, that there may be such cases I gladly recognize.

Whenever the tendon of the long head is retracted into the brachium somewhat from yielding of the secondary attachments before, or from retraction of the tendon after, rupture of the weakened intra-articular portion, the brachial part of the tendon is longer, and marked asymmetry between the position of the two muscle bellies of the biceps necessarily results and is intensified whenever the lateral belly atrophies because of elongation of the tendon.

No one sufficiently familiar with the evidence present in cadavers with respect to these lesions of the shoulder and others present through-

out the entire human body can have any doubt as to their significance. Indeed, the only phenomenon which still perplexes me is the exact manner of detachment of the subscapularis tendon from its insertion to the lesser tuberosity, for the middle portion of this tendon may be detached when the rest of it still remains attached by a peripheral ring of fine cylindric tendinous fasciculi, and complete detachment of the tendon from the lesser tuberosity may be present in cases of the developmental absence of the lateral belly of the biceps brachii. In some instances, too, only a few thin ribbon-like bands of tendon remain attached at intervals from above downward on this tuberosity. Such cases as these are rather puzzling, but they are that no matter what one may regard as causative factors in detachment of this tendon. Since atrophy of the tuberosity occurs in the areas of detachment of the tendon, it is possible that this absorption plays a rôle in the production of these anomalous detachments. Moreover, since the blood supply of tendons comes almost wholly from without, it follows that the destruction of the enveloping sheath must affect the firmness of attachment of the tendon in the course of time. Sharp or irregular portions of the cartilaginous margin of the head of the humerus, the osteogenetic reactions evoked in the traumatized periosteum and the absorption of cartilage no longer subjected to pressure from the tendon of the long head, all may be factors in the production of these detachments of the tendon of the subscapularis. Although the lesser tuberosity sometimes is normal in size and smoothness and covered with a thickened periosteum after the detachment of this portion of the insertion of the tendon of the subscapularis, it may be decidedly pitted and covered by an exceedingly thin periosteum or show little evidence of atrophy and be roughened by numerous low exostoses.

I have often wondered whether dislocations of the shoulder are not commoner in cases of maximal destruction from attrition and whether in some cases habitual dislocation may not be due to it, but I never have encountered such a condition in the dissecting room. However, since the stability of the shoulder joint depends so largely on muscles and tendons, it would seem that partial or complete destruction of the tendon of the supraspinatus and partial destruction of that of the infraspinatus accompanied by loss of the tubercular attachment of the subscapularis tendon must seriously reduce the stability of the joint even if not markedly affect its functional activity.

It seems that it should be possible to notice the presence of bony contacts in all cases in which this has become possible in consequence of capsular and tendinous or cartilaginous attrition. From my experience in auscultation of various supposedly normal articulations during movements which required no special strain, I am led to believe that

more can be made of this method of examination. It would also seem that the gap between the acromion and the head of the humerus indicated in roentgenograms must be reduced whenever the capsule or the articular cartilage on the head of the humerus or both are destroyed. Under the relaxation of deep general anesthesia, it should also be possible to produce a tap by forcing the head of the humerus against the lower surface of the acromion in all cases of large capsular defects. Although functional disabilities may be very misleading, some of them nevertheless must be suggestive with regard to both the extent and the character of the lesions present.

It is true that the literature on conditions of the shoulder plainly suggests that some of the symptoms, signs and disabilities accompanying the trauma of attrition have been attributed to dislocation, rheumatic arthritis, arthritis deformans, rupture, neuritis, periarthrititis, bursitis, tendinitis, senile necrosis, wear following disease and the effect of sudden motion, but that is an inference not based on personal knowledge of the cases concerned. The implication is not, to be sure, that none of the conditions mentioned can cause changes in and about the shoulder joint but that there may be profound changes without the presence of any of the foregoing conditions except that of wear.

REVIEW OF LITERATURE

Any one who has dissected a series of human bodies or has carefully observed their dissection must have encountered some, even if not all, of the foregoing lesions. Indeed, there is ample evidence in the medical literature to show that occasional observers have tried to explain very similar even if not identical phenomena, although Smith¹² thought that they have been "entirely overlooked . . . from inadvertency or other causes . . . in the ordinary dissection of bodies." During the dissection of forty bodies, Smith observed seven instances of destruction of the upper part of the capsule of the shoulder joint, destruction of part of the long tendon of the biceps and detachment of the tendon of the subscapularis and concluded that they were due to external factors such as a blow or fall, but he thoughtfully added:

It is a curious fact, that in two instances both joints of the same individual should have presented nearly similar appearances, and that the same cause should probably have produced exactly similar results [p. 222].

According to Smith:

The separation of the tendon of the subscapularis muscle from the lesser tubercle, (excepting in one case), where it was only partially torn away, may

12. Smith, John G.: Pathological Appearances of Seven Cases of Injury of the Shoulder Joints, with Remarks, *Quart. Periscope, Am. J. M. Sc.* **16**:219-224 (May) 1835; *London M. Gaz.* **14**:280-285, 1834.

be looked upon as the common result of the accident which produced these appearances; not so, however, with the tendons of the supra and infra-spinatus, and the teres minor muscles, from the greater tubercle, which appear to be more uncertain. In two instances all three tendons were torn away; in three cases only the tendon of the supra-spinatus; and in the remaining two cases, the whole of the tendons preserved their natural attachments [p. 222].

Callaway,¹³ like Smith, stated explicitly that what he observed were cases of traumatic rupture and dislocation of the tendon of the long head of the biceps muscle, and Rapp,¹⁴ who used the significant and appropriate word *Usur* in connection with lesions of the tendon of the long head of the biceps and who also represented the proximal portion of the torn tendon with a brushlike, free extremity as shown in figure 11, regarded this as due to growth after injury and concluded that luxations, disturbance of the circulation in the tendon sheath and inflammation may cause changes in the normal tendon of the biceps such as he encountered and the significance of which he was considering.

One of the historically most interesting and significant discussions of conditions in the shoulder is presented in an article by Robert Adams,¹⁵ which appeared in Todd's "Cyclopaedia of Anatomy and Physiology." Under the subhead of "chronic rheumatic arthritis of the shoulder joint," a "slow chronic disease" which "itself never causes death," Adams described many lesions such as those considered here, including destruction of the upper portion of the articular capsule; division, dislocation and reattachment of the long head of the biceps muscle; local destruction of the articular cartilages; destruction of the deeper portion of the capsule of the acromioclavicular articulation, and polishing of the head and tuberosities of the humerus and of the under surfaces of the acromial and coracoid processes. However, Adams also reported and included enlargement of the bones of the shoulder; thickening and enlargement of the articular capsule with adhesions to the acromion, coracoid process and the head of the humerus; frequent complete transverse division of the acromion within an inch of its extremity; effusions into the articular capsule with the presence of osseous fragments, and dislocation of the head of the humerus upward beyond the level of the clavicle and acromion and "completely backward on the dorsum of the scapula." The illustrations accompanying Adams'

13. Callaway, Thomas: A Dissertation upon Dislocations and Fractures of the Clavicle and Shoulder-Joint, Jacksonian Prize Essay for 1846, London, S. Highley, 1849, p. 178; reviewed, *Lancet* 2:400-401, 1849.

14. Rapp, Hermann: Ueber die Usur der Sehne des langen Kopfes vom M. Biceps brachii, Dissert., Tübingen, 1866.

15. Adams, Robert: Shoulder Joint, in Todd, R. B.: *Cyclopaedia of Anatomy and Physiology*, London, Longman [and others], 1852, vol. 4, pp. 571-621. Although this volume appeared in 1852, the text plainly implies that the article was written in 1848.

article show the presence of extensive articular exostoses and pronounced osseous extensions, such as are seen in so-called arthritis or arthrosis deformans. He emphasized the presence of "rheumatic arthritis" in practically all joints in his cases and believed that the case of Cruveilhier, in which ". . . the external extremity of the clavicle and the neighboring part of the acromion were in a great part destroyed," likewise belonged in the same category. Adams thought that "absorption" of the articular cartilages, both hyaline and fibroid, was effected by contact with capsular fimbria or so-called synovial villi, but recognized the presence of friction under such pathologic conditions.

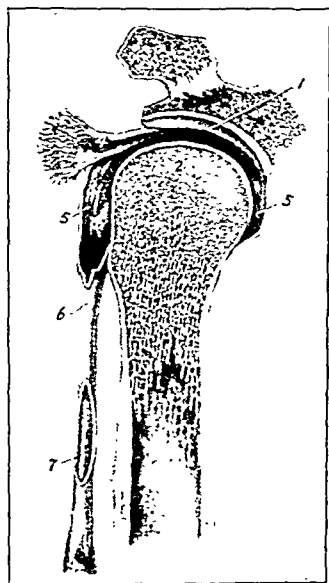


Fig. 11.—Sagittal section of a right shoulder. The glenoid cavity of the scapula is indicated by 1, the head of the humerus by 2, the tear and partly an outgrowth of the upper end of the tendon of the long head of the biceps by 3, the long head of the biceps by 4, the synovial capsule of the shoulder by 5 and the tendon sheath of the long tendon of the biceps by 6. The last-mentioned structure contains a sequestrum of the original tendon, indicated by 7. Those familiar with attrition effects will recognize that 3 is due neither to tear nor to growth. (After Rapp.¹⁴)

He thought, however, that "no doubt some few cases of chronic rheumatic arthritis of the shoulder joint in the living and in the dead have been mistaken for *partial dislocation of the head of the humerus, the results of accident . . .*" He was ". . . convinced that all these phenomena combined should by no means be considered as proof of any accident having occurred to produce them; but, on the contrary, should be looked upon as the usual result of chronic rheumatic arthritis

of the shoulder." He emphasized that in 1836 he had called attention to the fact that appearances delineated by Sir Astley Cooper in his treatise on "Fractures and Dislocations" corresponded exactly to the appearances found in the cases of "chronic rheumatic arthritis" and that all his subsequent experience "amply confirmed" this opinion, adding that he ". . . thought it necessary to enter into this subject thus minutely, because we are convinced that, up to the present hour, these remarkable appearances, when met with, have been misunderstood even by some of the most intelligent anatomists and physicians."

In the well known "Treatise on the Human Skeleton Including the Joints" by Humphry,¹⁵ some similar lesions were likewise mentioned, for when considering defects in the long tendon of the biceps, Humphry wrote:

The rent most often happens about half an inch from its glenoid attachment; and is most frequent in elderly persons, in whom the tendon becomes thin, in whom the synovial fluid is rather scanty, and in whom other changes, attendants on chronic rheumatism, are likely to be in progress.

I do not know of any evidence in support of the assumption that tendons become thin and synovia scanty, under the conditions concerned here, but Humphry very significantly said:

Under these circumstances there can be no doubt that the tendon sometimes becomes *worn through* by the friction of the head of the humerus upon it; and I quite agree with the writer in the Cyclopædia of Anatomy [Adams], that many of the specimens, in which the biceps tendon stops short in the bicipital groove, or becomes lost in the capsule of the joint, are to be attributed, not to rupture of the tendon, but to the continued effects of chronic rheumatism, originating in an accident, or commencing spontaneously [p. 415].

It is noteworthy that Humphry added the following in a footnote:

It would appear, from some dissections of the shoulder-joint described by Mr. J. G. Smith, *Medical Gazette*, XIV. p. 280, that, not only may the tendon of the biceps be worn through, but that the capsular ligament and the tendons of the supra- and infra-spinatus muscles may undergo the same change, and the sub-deltoid bursa thus become opened into the cavity of the joint. In several of the cases mentioned the sub-scapularis tendon was more or less detached from the lesser tubercle. Mr. Smith regards these changes as the result of accident; but several other points in the state of the joints, and the existence of similar conditions in both shoulders of the same person, render it more probable that they were the gradual result of friction and chronic rheumatism.

It is of interest in this connection to recall that Sir W. Arbuthnot Lane¹⁷ thought ". . . that the pressure which in elderly subjects

15. Humphry, George Murray: A Treatise on the Human Skeleton Including the Joints, Cambridge, Macmillan & Co., 1858.

17. Lane, W. Arbuthnot: A Remarkable Example of the Manner in Which Pressure-Changes in the Skeleton May Reveal the Labour-History of the Individual, *J. Anat. & Physiol.* 21:385-406, 1887.

or in those of low vitality destroys the articular cartilage and the subjacent bone, rendering the latter eburnated, and determining the formation of additamentary bones, produces in a young subject a similar alteration in the form of the articular surface, without affecting the vitality or continuity of its cartilaginous covering" (p. 386). He thought that ". . . pressure-changes in the skeleton may enable us to detect the habits and labour-history of the individual" (p. 386) and concluded regarding one case that "during the whole of his active life this man had been continually occupied in shovelling some material which was very coarse . . ." (p. 398). Sir Arbuthnot also spoke of a case in which ". . . the glenoid ligament was separated completely from the upper third of the margin of the glenoid cavity, being connected to it indirectly by a thin membrane. The upper part of the glenoid cavity was slightly increased in area. The cartilage covering the lower part had been converted into synovial membrane and areolar tissue . . ." (p. 388). He attributed these things to an "upward displacement of the head of the humerus which ensues in old age. . . ." (p. 388), but he recognized that bone may be removed as a result of "friction and pressure" and thought that pressure from the radial head of the humerus on the head of the radius may cause polishing and eburnation (p. 389). He offered this explanation also for perforated or wholly destroyed articular cartilage at the distal extremity of the ulna (p. 390) and believed that he had "shown that constant pressure exerted by the inferior articular processes of the 4th lumbar vertebra, and by the superior articular processes of the sacrum upon that portion of the arch of the 5th lumbar vertebra which lies between their extremities, may cause its partial or complete section" (p. 398). After considerable discussion of this matter, Lane referred to two cases of this anomaly reported by Professor Neugebauer, which the latter said were very puzzling and which he ascribed to congenital causes (p. 400). Although Lane also referred to an article by Sir W. Turner in which the latter described "several cases of want of union of the neural arch with the body of the 5th lumbar vertebra, which he ascribes to imperfect development" (p. 401), Lane nevertheless held to his opinion as to the origin of these anomalies and said ". . . *that the causation of the condition is pressure and not fracture, or a non-union of bony centres*" (p. 401).

These quotations pointedly reveal the significance of the older literature, in which a fall, blow, fracture, dislocation or disease, especially arthritis, is usually assigned as cause for the lesions encountered. It is largely for this reason that I have not discussed that literature fully, for it ill becomes one who did not even see the cases described by others

to question the correctness of their interpretations. A fine summary of the extensive older literature is given by Gilcreest.^{18c}

Codman, who has given so much attention to painful shoulders, thought that a hole in the humeroscapular capsule might close completely and stated ¹⁸ that he put a good many silk "sutures à-distance" between the separated ruptured ends of a supraspinatus tendon, because ". . . it seemed possible for repair to take place along the silk sutures." No one will deny that a rupture in a normal capsule or tendon may heal provided the torn ends are in direct or indirect apposition and are put at rest immediately, but Dr. Codman stated that he never operated in any case until three weeks after rupture, and since the period given apparently was inferred there is no assurance that it may not have been three months after. Moreover, I infer that he believes that defects which are the result of wear, such as I am considering here, also may heal, for he said ⁵ (p. 86) that the triangular defects in the supraspinatus tendon always become rounded, as does a defect in the epithelium of the skin, "before it heals" and that incomplete ruptures (those in which the rent in the tendon is from $\frac{1}{4}$ to $\frac{1}{2}$ inch [0.6 to 1.3 cm.] in length) will heal of themselves. Codman had also suggested earlier that clipping away the "inflamed" bursa over the ruptured tendon would cause satisfactory healing, but he ⁵ later doubted this (p. 131).

Wilson ¹⁹ considered only cases of complete rupture of the supraspinatus tendon with gaps up to "2½ inches in diameter." [!] He spoke of the presence of "fibrillation of the tendon and shredding with the formation of irregular tabs of tissue, sometimes calcified," and "occasionally fibrillation" of the articular cartilage on the head of the humerus as being most evident in patients in whom the longest time had elapsed since injury. Wilson found no pathologic changes present at the time of operation but said that the greater tuberosity is usually "bare" of tissue. If so, it follows that the distal stub of the ruptured tendon must have been completely resorbed in the interval between the accident and the operation, and if the greater tuberosity really was completely bare, it also is necessary to account for the absence of periosteum, which cannot be attributed to atrophy. On referring to some lesions of the shoulder reported by me and the suggested explanation for them, Wilson correctly said that "Most of his investigations have been made on dissecting room subjects," but he nevertheless added that these ". . . must have been cases of rupture of the supraspinatus tendon." [!]

18. Codman E. A.: Complete Rupture of the Supraspinatus Tendon: Operative Treatment with Report of Two Successful Cases, Boston M. & S. J. **164**:708-710, 1911.

19. Wilson, Philip D.: Complete Rupture of the Supraspinatus Tendon, J. A. M. A. **96**:433-439 (Feb. 7) 1931.

Although Keyes²⁰ found almost complete obliteration of the subdeltoid bursa by fibrous adhesions which "resembled" those "in the peritoneal cavity, particularly in the pelvis of the female," and mentioned the presence of hypertrophic bony changes on the greater tuberosity and the adjacent regions, of deposits of calcium in the supraspinatus tendon, of increased fragility of the bone of the greater tubercle and of erosion of the articular surface of the humerus, he nevertheless emphasized that fraying of the tendon of the long head was not observed and that the tendon was intact in every instance, but in 1933 he²¹ said that all his cases "were associated with a certain amount of tendon fraying and bony irregularity" and assured readers that "this description of one lesion covers the main features of all the other . . ." of a series of fourteen of seventy-two cadavers, or nineteen of one hundred and forty-two shoulders. A larger series of observations would undoubtedly have revealed greater variations among them.

Keyes also said, in 1933, that the tendon of the supraspinatus muscle "during the terminal half of its course [6 cm. according to Keyes] . . . is inseparable from the joint capsule," and that "its two borders may be distinguished from the adjoining borders of the tendon of the infraspinatus and subscapularis only with some difficulty. . . ." He added that rupture of the supraspinatus tendon "is related to subdeltoid or subacromial bursitis;" that the lesions considered by him were due to "some process . . . which progressed with years, gradually causing degeneration first of the floor of the subacromial bursa, then wearing through the tendon at its insertion into the greater tubercle, and finally causing a perforation or rupture of the tendon." However, in 1935 Keyes thought that the lesions were "traumatic and degenerative in nature" and that "age, long use, and trauma seemed the chief causative factors," although "alterations in tissue growth and metabolism were believed to act locally" He added that infection caused the changes seen in few of these shoulders. Keyes also reported the absence of atrophy of the supraspinatus muscle "even when a large rupture [up to 2.2 cm. wide by 3.5 cm. long] was present in its tendon"

Any one who has microscopically or even macroscopically examined the borders of the capsular defects I am considering must realize that spontaneous healing is absolutely out of the question, no matter what the size of the defect or the degree of use of the arm, for in order that healing may occur it is necessary not only that the edges of the defect

20. Keyes, E. Lawrence: Anatomical Observations on Senile Changes in the Shoulder, *J. Bone & Joint Surg.* **17**:953-960, 1935.

21. Keyes, E. Lawrence: Observations on Rupture of the Supraspinatus Tendon, Based upon a Study of Seventy-Three Cadavers, *Ann. Surg.* **97**:849-856, 1933.

be freshened and brought together but that the structures be put at rest. The mere presence of fluid or even of a coagulum between the widely separated ends of tendons divided by attrition weeks and months previously would not evoke or facilitate the least reparation and the startling suggestion that such reparation might occur along silk sutures between the widely separated ends of a tendon or capsule does not seem to rest on a sound basis.

I am reminded that Codman and Akerson,²² writing on "The Pathology Associated with Rupture of the Supraspinatus Tendon," said that it is the usual cause of traumatic subacromial (subdeltoid) bursitis. I am at present writing a book to support this contention [p. 353]. . . . The large number of bilateral cases (fourteen) found at autopsy speaks against traumatism and in favor of some form of slow necrotic destruction" [p. 356]. It is important to note that Codman and Akerson apparently found no pathologic condition responsible for the alleged rupture of the tendon of the supraspinatus, and since bursitis is assumed to follow its rupture it manifestly cannot be a factor in its production. The only other pathologic process postulated is a "slow necrotic destruction" for the occurrence of which Codman and Akerson seem to have found no postmortem evidence except the presence of alleged rupture which the necrotic changes were supposed to cause.

It is important to note that Codman and Akerson gained their information on cadavers through "a cut . . . made on the anterior aspect of the shoulder-joint from the acromioclavicular articulation downward for about two inches" (p. 352). Any one who has followed careful dissections of the shoulder will recognize how inadequate such a method of postmortem examination is for revealing the true conditions in the joint. I admit that some one may examine a single shoulder thoroughly and come to a correct conclusion regarding the condition but scarcely on evidence obtained from inspection through a 2 inch (5 cm.) incision at autopsy.

I am wholly at a loss to understand how these authors could hold that "a purely anatomic argument against Doctor Meyer's theory is that the impingement of the head of the humerus on the lower surface of the acromion does not occur in the normal individual" (p. 357), for I certainly implied nothing of the sort. It does not require a lifetime in the dissecting room to apprise one of the fact that the head of the humerus is not in direct contact with the acromion when the joint capsule is intact! Moreover, the two sentences which follow the one just quoted are equally perplexing and unintelligible, for Codman and Akerson wrote: "The friction at this point is taken up by the outer

22. Codman, Ernest A., and Akerson, Irving B.: *The Pathology Associated with Rupture of the Supraspinatus Tendon*, *Ann. Surg.* 93:348-359, 1931.

side of the tuberosity which is covered with the lower surface of the bursa. Furthermore, the coraco-acromial ligament partially intervenes"—evidently between the head of the humerus and the acromion! It is difficult to see why the shoulder joint ". . . is anatomically not likely to show the usual changes associated with arthritis" (p. 356) and that "from our understanding of accepted principles of pathology, such actual destruction by friction is well nigh impossible" (p. 357).

These authors further stated that "a feeble effort at repair" may result in ". . . the formation of a falciform edge (in the vertical plane) of fibrosynovial tissue which smooths the edge of the rupture around the whole circumference [pp. 354-355] . . . The rents in the other tendons extend laterally from that in the supraspinatus, even to the extent of evulsion of all of the tendons of the short rotators" [p. 356]. Certainly, no one will deny that all the tendons of the short rotator muscles may be evulsed, but surely not without a history of serious trauma and recourse on the part of the patient to immediate treatment, thus throwing the condition wholly outside of the category of those that I considered and attributed to attrition.

It is noteworthy that Codman, who has given so much and such long attention to these matters in living subjects, said in 1934⁵ (p. 84) that although he enjoyed the cooperation of friends he never saw a fresh rupture of the supraspinatus tendon on the operating table or at autopsy and never operated on a *young* man and "demonstrated" the presence of a ruptured tendon. The average age in his series of patients with assumed complete rupture of the supraspinatus tendon was 55, and of partial rupture, 49 years! The fact that none of the cases of so-called rupture mentioned by Codman occurred before the age of 50 and that none came to his attention for weeks or months after the presumed rupture surely is of great significance and cannot be explained by Codman's belief that partial acute ruptures are painless.

Codman regarded all communications between the subdeltoid bursa and the joint cavity as "pathologic" and suggested arthritis, periarthritis, bursitis, chronic inflammation and possibly overuse as causes for rupture of the tendon of the supraspinatus muscle. Yet he expressed the belief (p. 97) that rupture of this tendon is usually caused by sudden elevation of the arm, not under a load but merely in order to maintain body balance when in a drunken state! This idea was emphasized further on page 134, where it is said that "adequate injury—usually a fall" is responsible for the rupture.

Although bony excrescences were present in the case shown in his figure 3, plate 4, Codman stated that he found no evidences of pathologic changes, but on page 108 it is stated that he now believes that trauma and arthritis play alternating parts and (p. 109) that "some toxic

disturbance" may render the "joint tissues and the adjacent tendons sub-normal, and even partially necrotic, so that slight traumata which would not affect a normal tendon, easily tore their fibers." On page 112 of this same work it is said that:

. . . it is fair to postulate that most of the operative cases had some degree of "arthritic" degeneration in their musculo-tendinous cuffs before their accidents (p. 112). . . . When I first began my work on "Stiff and Painful Shoulders," the usual diagnosis assigned to such cases was "peri-arthritis." Following my articles drawing attention to the anatomic characteristics of the bursa and the importance of its recognition, the term "subdeltoid bursitis" replaced that of "peri-arthritis," and since my second paper, the adjective "subacromial" has largely replaced that of "subdeltoid" (p. 119); . . . we might say with much truth that there is no such condition as a chronic arthritis *per se* of the shoulder, for, owing to the structure of the joint, it would always be a peri-arthritis; . . . I contend that the defects in this cuff so frequently found at autopsy were originally largely traumatic, although unhealthy tendon may have suffered the trauma (pp. 117-118), . . . tendinitis both of the calcified and uncalcified forms precedes the peaks of incidence of the ruptures, partial and complete, by about five to ten years (p. 138).

According to Codman (p. 122), complete rupture of the supraspinatus tendon causes a chronic bursitis, and inflammation of the tendon probably remains painless until a subacromial bursa becomes involved. He further expressed the belief (p. 121) that hyperabduction of an arm for a period of one to two hours may cause a bursitis which may last for half a year; that²³ the strain on the subdeltoid bursa in operations on the breast may cause bursitis; that this is the rule rather than the exception, and that "brachial neuritis" usually is a bursitis.

Excellent evidence against the assumption that the lesions I have considered are pathologic in origin is afforded by the cartilaginous changes observed by Glauning²⁴ in the knee joints of horses. Except in two respects, these were wholly comparable to those found in the human being, and Glauning stated that none of the animals had been lame and that the changes observed were not due to inflammatory conditions. This is in accord with the findings in worn human tissues from the dissecting room which likewise revealed no evidences of disease.

23. Codman, Ernest A.: Rupture of the Supraspinatus Tendon. *Surg., Gynec. & Obst.* 52:579-586, 1931.

24. Glauning, Werner: *Altersveränderungen im Kniegelenk des Pferdes.* Inaug. Dissert., Habbel, Regensburg, 1936.

INFLUENCE OF LAPAROTOMY ON THE GASTRIC MOTOR MECHANISM OF MAN

LOUIS E. BARRON, M.D.

NEW HAVEN, CONN.

AND

GEORGE M. CURTIS, M.D.

AND

BERNARD LAUER, A.B.

COLUMBUS, OHIO

Disturbances in the motility of the stomach are frequently encountered after laparotomy. These may become of serious import if the underlying morbid process is not corrected. In this respect an understanding of the perverted physiologic activities of the human stomach is of peculiar importance, for without it therapy is uncertain and may prove to be unsuccessful.

To investigate certain of the problems which arise concerning pathologic gastric physiologic activity, preliminary observations were made on the influence of the extrinsic innervation on the motility of the human stomach. Unusual opportunities were available for studying the effect of resection of the splanchnic and of the vagus nerves on the gastric motor function. The surgical indications, the apparatus used and an analysis of the results obtained have already been reported.¹ The results of these fundamental observations led us to make an analysis of certain abnormal gastric manifestations so frequently encountered after laparotomy. The purpose of this paper is to report the results of this investigation.

METHOD OF INVESTIGATION

Gastric motility was studied in seven patients. Two presented cholecystitis associated with cholelithiasis for which cholecystectomy was eventually performed with the patients under nitrous oxide-ether anesthesia. Five were operated on for inguinal hernia. In this group spinal anesthesia was used for four patients and nitrous oxide-ether anesthesia for the fifth.

In the first group both patients presented the findings characteristic of disease of the biliary tract. Roentgenographic studies revealed in one patient numerous

From the Department of Surgery, Yale University School of Medicine, and the Department of Research Surgery, Ohio State University.

1. Barron, Louis E.; Curtis, George M., and Haverfield, William T.: The Effect of Bilateral Resection of the Splanchnic Nerves on Gastric Motility in Man, *Arch. Surg.* **32**:577 (April) 1936. Barron, Louis E.; Curtis, George M.; Haverfield, W. T., and Lauer, B.: Effect of Vagotomy on the Gastric Motor Mechanism of Man, *ibid.* **34**:1132 (June) 1937.

opaque shadows suggestive of facettated gallstones. In the other there was non-visualization of the gallbladder after the intravenous administration of the dye. The diagnosis of cholecystitis associated with cholelithiasis was confirmed for both patients at operation.

Tracings of the gastric motility were made during prolonged preoperative control periods. Observations were resumed as soon as postoperative nausea and vomiting subsided. This was approximately four days after cholecystectomy.

In the second group one patient presented bilateral indirect inguinal hernia. Herniorrhaphy was performed in two stages. Tracings of the gastric motility were made during the preoperative control period, during the first operation and throughout an intervening ten day period and were resumed subsequent to the second operation. It thus became possible to compare the results of two separate but similar operations on the same patient. Since spinal anesthesia was employed for four patients, tracings of the gastric motility were possible during the actual hernial repair as well as immediately after the surgical procedure. Daily observations were continued on all patients until they were discharged from the hospital.

Gastric motility was investigated by the balloon and kymograph method. The specific details of this procedure and the manner of ascertaining the position of the balloon in the stomach, as well as the method of analyzing the results, have been described.¹ Observations were made in the morning about fourteen hours after the evening meal. The usual duration of each continuous observation was about five hours. Tracings of the gastric motility were also made on the morning of operation to note any disturbances in motility possibly associated with emotional changes resulting from anticipation of the surgical procedure.

The specific criteria for the evaluation of gastric motility were essentially the same as those described in the earlier reports.¹ The data obtained from each patient were similarly arranged in tabulated form to facilitate accurate comparative study. Those appearing in this paper are representative. In a few instances a signal magnet and electric key were incorporated into the system. The patients were instructed to indicate any abdominal discomfort by pressing the key, which in turn produced an informative mark on the tracing, thereby making it possible to note any correlation between the abdominal symptoms and the results appearing on the kymographic record.

RESULTS

When the results of this investigation were surveyed in their entirety, it was evident that variation was present. It would seem that the specific disease, its duration and the eventual surgical management were responsible, at least in part, for this. As a consequence, the results are presented with reference to the primary disease and its subsequent therapy.

Cholecystitis with Cholelithiasis.—During the preoperative control period the duration of periods of motility was somewhat increased (table 1). In many instances they persisted for more than one hundred minutes (fig. 1). Frequently mild epigastric pain was experienced during this prolonged period of gastric activity. By means of the electric key and signal magnet, it appeared that this abdominal discomfort accompanied intense gastric contractions.

TABLE 1.—Analysis of Experiments on Gastric Motility During the Control Period in a Case of Cholecystitis with Cholelithiasis

Date of Experiment	Duration of Experiment	Periods of Quiescence		Periods of Activity		Contractions				Comment	
		No.	Duration	No.	Duration	Type	No.	Duration	Interval Between		Amplitude
5/25/35	4 hr.	1	29 m.	II	23	Max. 55 s.* Min. 20 s.	Max. 3 m. Min. 1 m.	Max. 5 cm. Min. 2.5 cm.	Terminated in tetany Fluctuations in tonus
		1	25 m.	1	77 m.	II	46	Max. 50 s. Min. 20 s.	Max. 3 m. Min. 10 s.	Max. 6 cm. Min. 2.5 cm.	
		1	169 m.	
5/26/35	4 hr., 45 m.*	1	29 m.	II	31	Max. 45 s. Min. 20 s.	Max. 1 m., 30 s. Min. 10 s.	Max. 4 cm. Min. 2 cm.	Terminated in tetany
		1	10 m.	1	120 m.	II	77	Max. 1 m. Min. 30 s.	Max. 4 m., 15 s. Min. 20 s.	Max. 4 cm. Min. 1.5 cm.	
		1	14 m.	1	70 m.	II	53	Max. 1 m. Min. 35 s.	Max. 2 m. Min. 40 s.	Max. 5 cm. Min. 2.5 cm.	
		1	14 m.	1	22 m.	II	17	Max. 45 s. Min. 20 s.	Max. 1 m., 20 s. Min. 55 s.	Max. 4 cm. Min. 2 cm.	
		1	11 m.	I	Inest- imable	Inestimable	Inestimable	Low grade	
5/29/35	5 hr.	1	7 m.	1	282 m.	II	300	Max. 1 m., 5 s. Min. 45 s.	Max. 1 m., 20 s. Min. 15 s.	Max. 3 cm. Min. 1.5 cm.	Symptoms of biliary colic
		1	17 m.	II	19	Max. 55 s. Min. 40 s.	Max. 40 s. Min. 5 s.	Max. 5.5 cm. Min. 2 cm.	
		1	14 m.	1	121 m.	II	58	Max. 55 s. Min. 35 s.	Max. 3 m. Min. 25 s.	Max. 5.5 cm. Min. 2.5 cm.	
5/29/35	1 hr.	1	24 m.	1	74 m.	II	58	Max. 55 s. Min. 30 s.	Max. 5 m. Min. 10 s.	Max. 5.5 cm. Min. 2.5 cm.	Continuous gastric motility throughout the observation period; symptoms and signs characteristic of biliary colic
		1	50 m.								

* In this and the following tables m. indicates minutes; s., seconds; Max., maximum, and Min., minimum.

An increase in the usual amplitude of contractions was also observed. Frequently this was as much as from 8 to 10 cm. (table 1). The interval between contractions was about two minutes, and the usual duration of each contraction was about one minute.

The duration of the period of gastric quiescence was variable and was attended by no epigastric distress. During such periods it was possible to observe low grade fluctuations in gastric tonus. Respiratory excursions were evident on the kymographic tracings. With the resumption of intense gastric motility there frequently ensued a recurrence of epigastric distress simultaneous with the severe contractions. In a few instances tracings were obtained during attacks of abdominal pain, which from the standpoint of intensity and radiation was char-

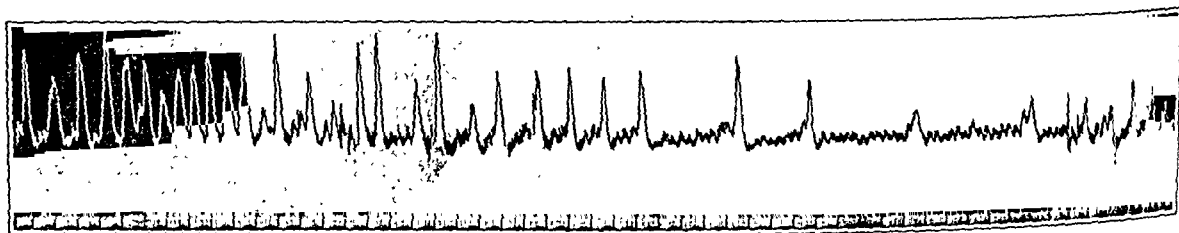


Fig. 1.—Tracing made on May 26, 1935, showing the persistence of gastric motility for one hundred and twenty minutes in a patient with untreated cholelithiasis.

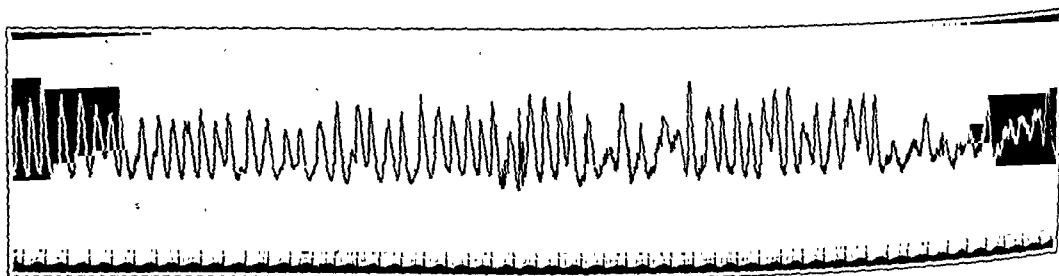


Fig. 2.—Tracing made on May 28, 1935, showing continuous gastric motility during biliary colic. The duration of this period was two hundred and eighty-two minutes.

acteristic of biliary colic. The gastric motility under such circumstances was continuous throughout observation periods of from four to five hours (fig. 2), during which severe contractions were occasionally noted.

The use of general anesthesia prohibited the study of gastric motility during cholecystectomy. However, on the morning of the fourth post-operative day studies were resumed and serial observations continued. These revealed definite hypermotility, more pronounced than that of the control period and persisting throughout an observation period of approximately three hours (fig. 3). The amplitude of the contractions was definitely increased (table 2).

Epigastric distress appeared to parallel these periods of hypermotility during which severe contractions were evident. At the termination of the observations the patients complained of abdominal discomfort, which was invariably interpreted as "gas pains" (fig. 3). Subjectively these sensations persisted for about a week after cholecystectomy. However, the hypermotility persisted for a longer period (table 2). As a late manifestation, the patients complained of intense hunger (fig. 4). The entire duration of the period of postoperative hypermotility was approximately three weeks. Subsequently the motility returned to normal.



Fig. 3.—Tracing made on June 4, 1935, four days after cholecystectomy, showing intense gastric motility persisting for one hundred and eighty-two minutes. At the termination of this period, the patient complained of "gas pains."

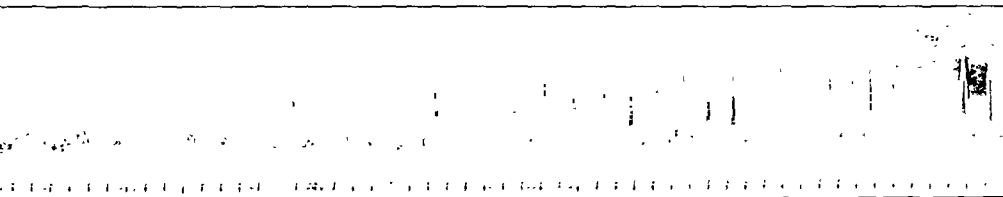


Fig. 4.—Tracing made on June 12, 1935, twelve days after cholecystectomy, showing intense gastric motility associated with hunger. The duration of this period was one hundred and forty-four minutes.

Herniorrhaphy.—Gastric motility was studied on five patients with inguinal hernia. Herniorrhaphy was eventually performed after adequate control studies (table 3). Tracings were also obtained on the morning of operation. On four patients records were made during the operative procedure, which was conducted with low spinal anesthesia. Studies were then resumed immediately after the repair. The duration of these periods of observation varied, but on the whole they were approximately four hours. Daily observations were then made in the morning until the patient was discharged from the hospital. The results were similar in all five patients.

TABLE 2.—*Analysis of Experiments on Gastric Motility After Cholecystectomy*

Date of Experiment	Duration of Experiment	Periods of Quiescence		Periods of Activity		Type	No.	Contractions			Comment
		No.	Duration	No.	Duration			Duration	Interval Between	Amplitude	
6/ 4/35	4 hr.	1	182 m.	II	132	Max. 1 m. Min. 25 s.	Max. 3 m., 10 s. Min. 55 s.	Max. 6 cm. Min. 2.5 cm.	Complained of gas pains
		1	13 m.	1	45 m.	II	27	Max. 50 s. Min. 20 s.	Max. 3 m., 20 s. Min. 55 s.	Max. 6 cm. Min. 3.5 cm.	
6/ 5/35	4 hr., 35 m.	1	104 m.	II	60	Max. 55 s. Min. 25 s.	Max. 5 m., 40 s. Min. 10 s.	Max. 6.5 cm. Min. 2 cm.	Complained of gas pains
		1	25 m.	1	75 m.	II	38	Max. 1 m. Min. 30 s.	Max. 4 m. Min. 35 s.	Max. 6.5 cm. Min. 3 cm.	
		1	16 m.	1	55 m.	II	20	Max. 50 s. Min. 20 s.	Max. 4 m., 15 s. Min. 1 m., 30 s.	Max. 6 cm. Min. 2.5 cm.	
6/ 6/35	4 hr., 50 m.	1	44 m.	II	35	Max. 1 m. Min. 15 s.	Max. 5 m., 20 s. Min. 20 s.	Max. 4.5 cm. Min. 2.5 cm.	Complained of gas pains
		1	22 m.	1	169 m.	II	121	Max. 55 s. Min. 35 s.	Max. 6 m. Min. 5 s.	Max. 6 cm. Min. 2.5 cm.	
		1	10 m.	1	45 m.	II	38	Max. 1 m., 20 s. Min. 30 s.	Max. 2 m., 15 s. Min. 40 s.	Max. 6 cm. Min. 2 cm.	
6/ 8/35	4 hr., 15 m.	1	50 m.	II	20	Max. 1 m. Min. 30 s.	Max. 5 m., 10 s. Min. 1 m.	Max. 5 cm. Min. 1.5 cm.	Complained of gas pains
		1	54 m.	1	20 m.	II	10	Max. 1 m. Min. 40 s.	Max. 3 m. Min. 35 s.	Max. 4.5 cm. Min. 1.5 cm.	
		1 1	12 m. 103 m.	1	16 m.	II	10	Max. 50 s. Min. 30 s.	Max. 2 m., 35 s. Min. 25 s.	Max. 4.5 cm. Min. 2 cm.	
6/10/35	2 hr., 30 m.	Continuous motility throughout observation period; patient complained of nausea and epigastric distress									
6/12/35	4 hr.	1	19 m.	II	23	Max. 1 m. Min. 20 s.	Max. 1 m. Min. 10 s.	Max. 4.5 cm. Min. 2.5 cm.	Complained of gas pains
		1	9 m.	1	144 m.	II	114	Max. 1 m. Min. 40 s.	Max. 2 m., 30 s. Min. 40 s.	Max. 5 cm. Min. 2.5 cm.	

6/13/35	3 hr.	1	9 m.	1	50 m.	II	36	Max. 45 s. Min. 20 s.	Max. 4 m. Min. 35 s.	Max. 4.5 cm. Min. 1.5 cm.	Complained of hunger
		1	13 m.	II	16	Max. 1 m. Min. 30 s.	Max. 1 m. Min. 5 s.	Max. 4 cm. Min. 2 cm.	
		1	9 m.	1	158 m.	II	92	Max. 1 m. Min. 45 s.	Max. 5 m. Min. 20 s.	Max. 5 cm. Min. 1.5 cm.	
6/15/35	3 hr.	1	7 m.	III	Inestl- mable	Inestimable	Inestimable	Gastric tetany
		1	5 m.	1	28 m.	II	25	Max. 50 s. Min. 10 s.	Max. 1 m. Min. 15 s.	Max. 4.5 cm. Min. 2 cm.	Terminated in tetany
		1	7 m.	1	133 m.	II	136	Max. 1 m. Min. 25 s.	Max. 1 m., 50 s. Min. 20 s.	Max. 5 cm. Min. 1.5 cm.	Complained of hunger
6/17/35	3 hr., 25 m.	1	9 m.	II	10	Max. 25 s. Min. 16 s.	Max. 20 s. Min. 5 s.	Max. 5 cm. Min. 2 cm.	
		1	5 m.	1	39 m.	II	42	Max. 50 s. Min. 20 s.	Max. 1 m. Min. 5 s.	Max. 4 cm. Min. 1.5 cm.	
		1	5 m.	1	147 m.	II	151	Max. 1 m. Min. 25 s.	Max. 1 m., 10 s. Min. 5 s.	Max. 4 cm. Min. 1.5 cm.	
6/18/35	3 hr., 5 m.	1	35 m.	II	22	Max. 35 s. Min. 25 s.	Max. 2 m. Min. 10 s.	Max. 5 cm. Min. 2 cm.	
		1	87 m.	1	63 m.	II	16	Max. 45 s. Min. 30 s.	Max. 3 m. Min. 1 m.	Max. 5.5 cm. Min. 2.5 cm.	Complained of hunger
6/19/35	3 hr.,	1	88 m.	1	92 m.	II	32	Max. 40 s. Min. 10 s.	Max. 10 m. Min. 16 s.	Max. 5 cm. Min. 2 cm.	
6/20/35	4 hr., 35 m.	1	12 m.	II	0	Max. 1 m., 25 s. Min. 20 s.	Max. 1 m. Min. 10 s.	Max. 5 cm. Min. 3.5 cm.	
		1	99 m.	1	35 m.	II	23	Max. 45 s. Min. 20 s.	Max. 2 m., 40 s. Min. 20 s.	Max. 2.5 cm. Min. 2 cm.	
		1	75 m.	1	54 m.	II	17	Max. 45 s. Min. 10 s.	Max. 2 m., 45 s. Min. 1 m., 30 s.	Max. 3 cm. Min. 1.5 cm.	

TABLE 3.—*Analysis of Experiments on Gastric Motility During the Control Period in a Case of Right Indirect Inguinal Hernia*

Date of Experiment	Duration of Experiment	Periods of Quiescence		Periods of Activity		Contractions			Amplitude	Comment	
		No.	Duration	No.	Duration	Type	No.	Duration			Interval Between
11/ 9/35	4 hr., 40 m.	1	43 m.	I	Inestimable	Inestimable	Low grade		
		1	62 m.	1	36 m.	II	34	Max. 1 m., 5 s. Min. 20 s.	Max. 1 m., 20 s. Min. 5 s.	Max. 4 cm. Min. 2 cm.	
		1	48 m.	1	19 m.	II, III	Inestimable	Inestimable	Inestimable	Max. 4 cm. Min. 1.5 cm.	
		1	55 m.	1	17 m.	II	12	Max. 1 m. Min. 30 s.	Max. 1 m., 40 s. Min. 20 s.	Max. 3 cm. Min. 2 cm.	
11/11/35	4 hr.	1	62 m.	I, II	Inestimable	Inestimable	Max. 4 cm. Min. 1.5 cm.		
		1	62 m.	1	35 m.	II	35	Max. 1 m. Min. 15 s.	Max. 2 m. Min. 10 s.	Max. 4.5 cm. Min. 2 cm.	
		1	47 m.	1	22 m.	II	27	Max. 30 s. Min. 5 s.	Max. 1 m. Min. 5 s.	Max. 4 cm. Min. 1.5 cm.	Terminated in tetany
		1	12 m.								
11/12/35	4 hr., 30 m.	1	25 m.	II	18	Max. 30 s. Min. 10 s.	Max. 2 m. Min. 10 s.	Max. 4.5 cm. Min. 2 cm.	
		1	213 m.	1	35 m.	II	31	Max. 50 s. Min. 5 s.	Max. 1 m. Min. 5 s.	Max. 5 cm. Min. 2 cm.	
11/13/35	5 hr., 45 m.	1	23 m.	I	Inestimable	Inestimable	Max. 3 cm. Min. 2 cm.		
		1	59 m.	A few low grade contractions noted							
		1	51 m.	1	38 m.	I, II	Inestimable	Inestimable	Inestimable	Max. 4 cm. Min. 1.5 cm.	
		1	41 m.	1	54 m.	II	40	Max. 1 m. Min. 5 s.	Max. 2 m., 30 s. Min. 5 s.	Max. 5 cm. Min. 2 cm.	
		1	79 m.	Fluctuations in tonus

11/14/35	5 hr., 45 m.	1	48 m.	I, II	Inesti- mable	Inestimable	Inestimable	Max. 4 cm. Min. 1.5 cm.	Terminated in tetany	
		1	27 m.	1	20 m.	I, II	Inesti- mable	Inestimable	Inestimable	Max. 2.5 cm. Min. 1.5 cm.		
		1	99 m.	1	41 m.	II	33	Max. 1 m., 30 s. Min. 5 s.	Max. 2 m. Min. 5 s.	Max. 4 cm. Min. 2 cm.		
		1	104 m.	Few contractions during this period								
11/15/35	5 hr., 30 m.	1	41 m.	I, II	Inesti- mable	Inestimable	Inestimable	Max. 4.5 cm. Min. 2 cm.	Terminated in tetany	
		1	41 m.	1	34 m.	II	33	Max. 1 m. Min. 5 s.	Max. 2 m., 30 s. Min. 5 s.	Max. 4 cm. Min. 1.5 cm.		
		1	70 m.	1	20 m.	II	25	Max. 50 s. Min. 5 s.	Max. 1 m. Min. 5 s.	Max. 4 cm. Min. 2 cm.		
		1	50 m.	1	32 m.	II	30	Max. 55 s. Min. 5 s.	Max. 1 m., 15 s. Min. 5 s.	Max. 5 cm. Min. 2.5 cm.		
		1	21 m.									
11/17/35	4 hr., 33 m.	1	34 m.	I, II	Inesti- mable	Inestimable	Inestimable	Max. 3.5 cm. Min. 1.5 cm.	Terminated in tetany	
		1	70 m.	1	35 m.	I, II	Inesti- mable	Inestimable	Inestimable	Max. 3.5 cm. Min. 1.5 cm.		
		1	54 m.	1	23 m.	I, II	Inesti- mable	Inestimable	Inestimable	Max. 4 cm. Min. 2 cm.		
		1	55 m.									
11/18/35	5 hr., 50 m.	1	10 m.	II, III	Inesti- mable	Inestimable	Inestimable	Max. 3.5 cm. Min. 1.5 cm.	Terminated in tetany	
		1	40 m.	1	18 m.	II, III	Inesti- mable	Inestimable	Inestimable	Max. 3.5 cm. Min. 1 cm.		
		1	61 m.	1	40 m.	II, III	Inesti- mable	Inestimable	Inestimable	Max. 3 cm. Min. 1 cm.		
		1	23 m	1	50 m.	II, III	Inesti- mable	Inestimable	Inestimable	Max. 4 cm. Min. 1.5 cm.		
		1	70 m.	1	28 m.	I, II	Inesti- mable	Inestimable	Inestimable	Max. 4.5 cm. Min. 2 cm.	Terminated in tetany	
		1	20 m.	II, III	Inesti- mable	Inestimable	Inestimable	Max. 4.5 cm. Min. 2.5 cm.		
11/19/35	3 hr., 15 m.	1	102 m.	1	21 m.	II, III	Inesti- mable	Inestimable	Inestimable	Max. 3 cm. Min. 2 cm.		Epigastric distress Terminated in tetany
		1	13 m.	Herniorrhaphy on right side at 10:15 a. m.; gastric inhibition throughout operation								

Gastric Motility During and After Herniorrhaphy on Right Side

Date of Experiment	Duration of Experiment	Periods of Quiescence		Periods of Activity		Type	No.	Duration	Contractions		Amplitude	Comment
		No.	Duration	No.	Duration				Interval Between	After herniorrhaphy		
11/19/35	3 hr., 30 m.	Gastric inhibition throughout observation period; tracing made immediately after herniorrhaphy							Max. 3.5 cm. Min. 1.5 cm.	Terminated in tetany		
11/20/35	3 hr., 5 m.	Continuous low grade motility; occasional contraction of high amplitude							Max. 3 cm. Min. 1 cm.	Complained of gas pains		
11/21/35	3 hr., 15 m.	Continuous low grade motility throughout observation period							Max. 4.5 cm. Min. 1.5 cm.	Complained of gas pains		
11/22/35	5 hr., 8 m.	1	17 m.	1	18 m.	II	19	Max. 1 m. Min. 5 s.	Max. 4.5 cm. Min. 1.5 cm.	Low grade		
		1	8 m.	1	45 m.	II	43	Inestimable	Inestimable			
		1	28 m.	1	179 m.	I, II	Inestimable	Inestimable	Max. 3.5 cm. Min. 1.5 cm.			
		1	1	29 m.	I	Inestimable	Inestimable	Max. 3 cm. Min. 1 cm.			
11/23/35	5 hr.	1	27 m.	1	23 m.	I, II	Inestimable	Inestimable	Max. 4 cm. Min. 20 s.	Max. 3.5 cm. Min. 1 cm.	Complained of gas pains	
		1	71 m.	1	34 m.	I	Inestimable	Inestimable	Max. 3.5 cm. Min. 1 cm.	Max. 4 cm. Min. 1.5 cm.	Terminated in tetany	
		1	30 m.	1	86 m.	II	50	Max. 1 m., 10 s. Min. 20 s.	Max. 1 m. Min. 5 s.	Max. 3.5 cm. Min. 1 cm.		
		1	1	28 m.	II	27	Max. 1 m., 30 s. Min. 5 s.	Max. 2 m. Min. 5 s.	Max. 3.5 cm. Min. 1.5 cm.		
11/24/35	4 hr.	1	56 m.	1	51 m.	II	38	Max. 2 m., 10 s. Min. 5 s.	Max. 2 m., 10 s. Min. 5 s.			
		1	75 m.	1	27 m.	II	20	Max. 2 m. Min. 5 s.				
11/25/35	5 hr., 15 m.	Continuous motility throughout observation period; patient complained of hunger										
11/26/35	4 hr., 20 m.	Continuous motility throughout observation period; patient complained of hunger										

11/27/35	5 hr.	1	38 m.	II, III	Instimable	Instimable	Instimable	Max. 3 cm. Min. 1 cm.
		1	27 m.	1	26 m.	I, II	Instimable	Instimable	Instimable	Max. 5 cm. Min. 1.5 cm.
		1	38 m.	1	51 m.	I	Instimable	Instimable	Instimable	Low grade
		1	50 m.	1	58 m.	I, II	Instimable	Instimable	Instimable	Max. 3.5 cm. Min. 1 cm.
11/29/35	4 hr.	1	45 m.	I	Instimable	Instimable	Instimable	Low grade
		1	63 m.	1	132 m.	I, II	Instimable	Instimable	Instimable	Max. 4.5 cm. Min. 1.5 cm.
11/30/35	5 hr., 5 m.	1	51 m.	I	Instimable	Instimable	Instimable	Low grade
		1	32 m.	1	31 m.	I	Instimable	Instimable	Instimable	Low grade
		1	30 m.	1	152 m.	I, II	Instimable	Instimable	Instimable	Max. 3 cm. Min. 1 cm.
12/ 2/35	5 hr., 25 m.	1	28 m.	I	Instimable	Instimable	Instimable	Low grade
		1	48 m.	1	21 m.	I, II	Instimable	Instimable	Instimable	Max. 3.5 cm. Min. 1.5 cm.
		1	50 m.	1	32 m.	I, II	Instimable	Instimable	Instimable	Max. 3.5 cm. Min. 1.5 cm.
		1	53 m.	1	41 m.	II	32	Max. 1 m., 10 s. Min. 5 s.	Max. 2 m., 20 s. Min. 5 s.	Max. 3.5 cm. Min. 1.5 cm.
		1	49 m.	1			Instimable	Instimable	Low grade
12/ 3/35	5 hr.	1	93 m.	I	Instimable	Instimable	Instimable	Low grade
		1	49 m.	1	95 m.	II	51	Max. 1 m., 50 s. Min. 5 s.	Max. 3 m. Min. 5 s.	Max. 4.5 cm. Min. 2 cm.
		1	58 m.	1			Instimable	Instimable	Low grade
12/ 4/35	1 hr., 15 m.	1	41 m.	I	Instimable	Instimable	Instimable	Max. 1.5 cm. Min. 1.5 cm.
		1	50 m.	1	86 m.	II	55	Max. 2 m. Min. 5 s.	Max. 3 m., 10 s. Min. 5 s.	Max. 1.5 cm. Min. 1.5 cm.
		1	78 m	1			Instimable	Instimable	Low grade

Complained of hunger

Complained of hunger

Complained of hunger

During the control period some variation was noted (table 3). However, the motility was essentially normal (fig. 5 *A*). Immediately preceding hernial repair there appeared to be a definite increase in the amplitude of the contractions, although in many instances the total duration of the periods of activity was relatively short (fig. 5 *B*). There was evidence of considerable associated emotional disturbance. The patients complained of epigastric distress. There was an apparent relationship between the emotional state and the hypermotility. When spinal anesthesia was induced, the stomach became quiescent. This inhibition of gastric motility, associated with a marked reduction in tonus, continued throughout the operation (fig. 5 *C*).

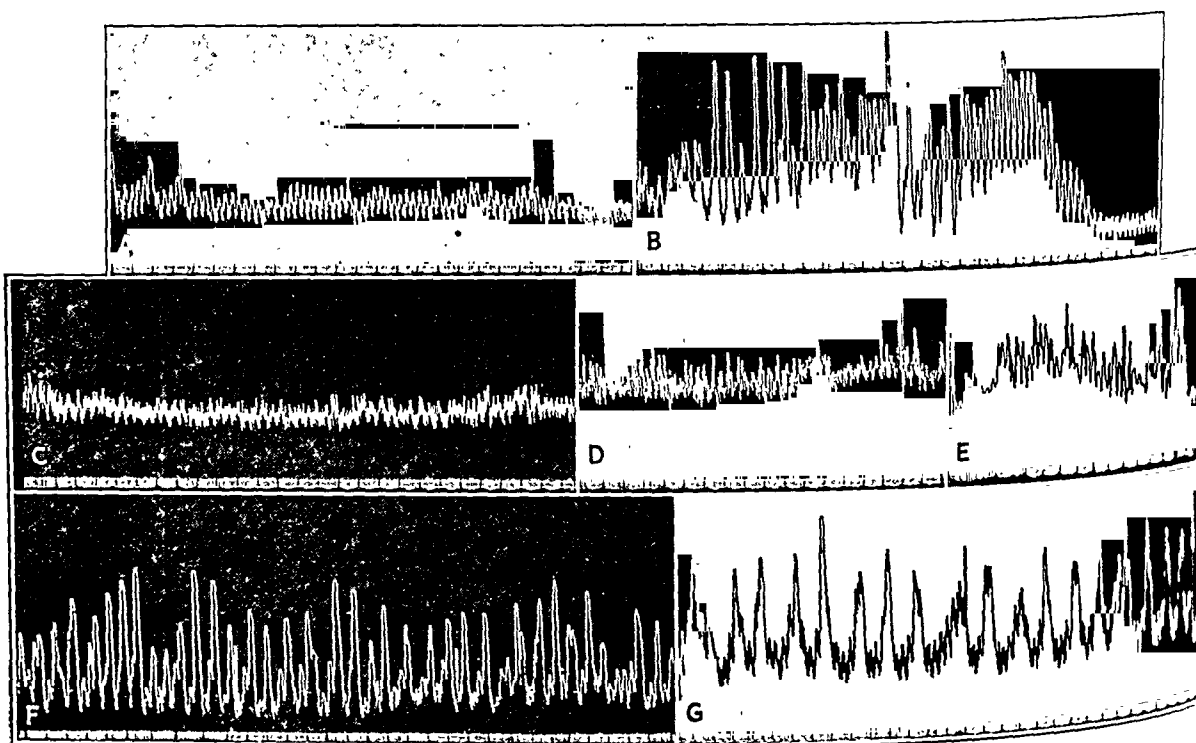


Fig. 5.—Sections *A* to *G* are segments of kymographic tracings obtained on the same patient. *A*, control tracing made on November 12, showing low grade gastric motility in a patient with right indirect inguinal hernia. *B*, tracing made on November 19, about an hour preceding herniorrhaphy. The gastric motility was intense but of short duration. *C*, tracing made on November 19, showing inhibition of the gastric motility during herniorrhaphy. *D*, tracing made on November 19, showing the persistence of inhibition for several hours subsequent to herniorrhaphy. *E*, tracing made on November 20, showing the return of gastric motility twenty-four hours subsequent to herniorrhaphy. *F*, tracing made on November 22, showing continuous motility with intense contractions three days after herniorrhaphy. The duration of this period was one hundred and seventy-nine minutes. At the termination of this observation the patient complained of "gas pains." *G*, tracing made on December 3, two weeks after herniorrhaphy, showing continuous gastric activity associated with hunger.

Inhibition of gastric motility persisted from twenty-four to approximately thirty-six hours subsequent to herniorrhaphy (fig. 5 *D*; table 4). In some instances it continued for seventy-two hours. After this period there was a gradual return of motility (fig. 5 *E*). This manifested itself first by an increase in tonus, superimposed on which were feeble contractions, which grew progressively more intense. About twenty-four to forty-eight hours after the onset of motility, definite hypermotility became evident (fig. 5 *F*). Simultaneous with this the patients complained of epigastric distress, interpreted by them as "gas pains." Hypermotility with intense contractions persisted for about two weeks. However, the sensation of "gas pains" was experienced for approximately one week after operation. Subsequently the patients complained of intense hunger as a late manifestation of hypermotility (fig. 5 *G*). Throughout the postoperative period medication was purposely avoided so that the results of laparotomy would not be obscured. In some patients the hypermotility persisted throughout their entire stay in the hospital. In others the motility approached the preoperative normal prior to discharge.

COMMENT

Preliminary observations on gastric motility revealed some variation among the patients. Therefore, a sufficient number of control studies was made in order to permit of adequate interpretations. The results from each patient were relatively uniform and essentially normal. They were in agreement with the results described by other investigators.²

Some evidence of hypermotility during the preoperative period is revealed in the two patients with cholecystitis. Although this was not constant, it was noted with sufficient frequency to be significant. Many tracings exhibited gastric contractions of abnormally great amplitude. When this occurred, the patients frequently complained of abdominal discomfort referable to the epigastrium.

The sensory mechanism which registers abdominal pain in disease of the gallbladder in the conscious patient is exceedingly complex. Theories describing the nervous pathways over which the sensory stimuli travel have been reported in detail elsewhere³ and therefore are intentionally omitted from this report. The abdominal pain to which we refer was always localized in the epigastrium and was interpreted as a dull, aching, boring distress. It was never associated with nausea or with vomiting. At no time did this discomfort reach sufficient

2. Carlson, A. J.: *The Control of Hunger in Health and Disease*. Chicago, University of Chicago Press, 1916.

3. Zollinger, Robert: Significance of Pain and Vomiting in Cholelithiasis, *J. A. M. A.* **105**:1647 (Nov. 23) 1935.

magnitude to indicate termination of the usual period of observation. It did not present the intensity or distribution characteristic of biliary colic.

The frequent occurrence of gastric hypermotility with its associated epigastric distress during the period of cholecystitis with cholelithiasis in which treatment was not given would suggest a relationship between disease of the biliary tract and reflex disturbances in gastric motor function. Carlson² made observations on the gastric motility of a patient with disease of the gallbladder. He, too, found that epigastric distress ran parallel with the strong contractions of the empty stomach. He also noted that the contractions were stronger than usual for the age of the patient.

This experimental evidence further indicates that in disease of the biliary tract there may be reflex stimulation of the gastric motor mechanism, with ensuing hypermotility of the stomach. Since epigastric distress accompanied the intense gastric contractions, it would seem that there also ensues a reflex stimulation of the sensory nerves of the stomach. However, the evidence is as yet too indefinite to permit the conclusion that gastric hypermotility is the sole cause of the abdominal distress concurrent with disease of the biliary tract. Doubtless other undetermined extragastric factors play a rôle. Nevertheless, the frequency with which hypermotility of the stomach was associated with epigastric distress in these two patients would indicate concomitant disturbances in reflex gastric motor and sensory functions. Carlson² noted that the epigastric pain often appeared greater than warranted by the strength of the gastric contractions. He expressed the opinion that infection of the gallbladder might lead to hyperexcitability of the sensory nervous mechanism of the stomach and duodenum, possibly from the spread of bacterial toxins along the branches of the vagus nerves.

Barber⁴ and Barber and Stewart⁵ also found hypermotility and pylorospasm associated with disease of the gallbladder. They reported that irritation of the gallbladder, duodenum and appendix increased the rate and force of the gastric contractions. Although the exact cause for this is not clear, it was thought to be of vagal origin.

In a few instances we obtained tracings of the gastric motility during attacks of biliary colic. These revealed continuous motility, frequently persisting throughout the period of observation. The amplitude of these contractions was about from 4 to 5 cm.

4. Barber, W. Howard: Gas and the Motility of the Surgical Stomach, *Ann. Surg.* 69:271, 1919.

5. Barber, W. Howard, and Stewart, George D.: Further Observations upon Reflex Gastric Hypermotility, *Proc. Soc. Exper. Biol. & Med.* 17:155, 1919-1920.

Various manifestations of abnormal gastric motor function have been described as associated with disease of the biliary tract; the most common observations have been pylorospasm and hypermotility of the stomach. McCrea⁶ reported that irritation and inflammation of the appendix or of the gallbladder may produce pylorospasm, gastric hypermotility and hyperchlorhydria. He even suggested that these may precede the development of ulcer. Smith and Miller⁷ demonstrated that irritation of the mucous membrane of the gallbladder of the anesthetized dog with croton oil was followed by a striking increase in the activity of the stomach. After the administration of atropine, there was a decrease in motility. Held and Roemer⁸ showed that disease of the gallbladder was likely to produce spasm of the pylorus with active peristalsis of the proximal portion of the stomach. They cited an instance in which gastrospasm was due to gallstones.

The mechanism responsible for the pylorospasm and gastric hypermotility is not clear. However, Hughson⁹ found that trauma to the abdominal viscera was capable of producing reflex contractions of the pylorus and gastric hypermotility. He also observed that as a result of peritoneal irritation there ensued an increase in the emptying time of the stomach which persisted for two weeks to a month. He advanced the hypothesis^{9b} that spasm of the pylorus resulting from disease either within or adjacent to the abdominal cavity is solely a result of irritation of the peritoneal surfaces.

Contrary to these findings, Ivy¹⁰ reported that mild stimulation of the biliary tract inhibited gastric motility and that distention of the biliary passages caused pylorospasm and also a marked delay in the evacuation of a barium sulfate meal. He noted that a sudden marked distention produced pylorospasm with nausea and vomiting. This was interpreted as being responsible for the dyspeptic symptoms of disease of the gallbladder. In his opinion the pain of biliary colic is not due

6. McCrea, E. D'Arcy: The Nerves of the Stomach and Their Relation to Surgery, *Brit. J. Surg.* **13**:621, 1926.

7. Smith, Fred M., and Miller, G. H.: A Study of the Reflex Influence of the Colon, Appendix and Gall Bladder on the Stomach, *Am. J. Physiol.* **90**:518, 1929.

8. Held, I. W., and Roemer, J.: Gastrospasm: A Clinical and Roentgenological Study, *Am. J. M. Sc.* **164**:188, 1922.

9. Hughson, Walter: (a) The Effect of Vagus Neurotomy on the Pyloric Sphincter: An Experimental Study, *J. A. M. A.* **88**:1072 (April 2) 1927; (b) Reflex Spasm of the Pylorus and Its Relation to Diseases of the Digestive Organs, *Arch. Surg.* **11**:136 (July) 1925.

10. Ivy, A. C.: (a) The Applied Physiology of the Gastro-Intestinal Innervation, *Am. J. Digest. Dis. & Nutrition* **1**:845, 1935; (b) Physiology of the Gall Bladder, *Physiol. Rev.* **14**:1, 1934.

to pylorospasm, because the type of referred pain is different, and pain referable to the biliary tract may be obtained in man and in the dog after subtotal gastrectomy.

The reports of various investigators thus indicate that pylorospasm is frequently associated with disease of the gallbladder. Whether this is due to local mechanism or to reflex action by way of the splanchnic or vagus nerves is not clear. However, it is well established that motor and inhibitory fibers enter the pylorus through the vagus and splanchnic nerves and that stimulation of either may result in pylorospasm.

Carlson and Litt¹¹ found that motor disturbances of the pylorus may be induced not only by local pathologic conditions in the stomach and duodenum or by abnormal states of the central nervous system but by excessive irritation of most, if not all, sensory nerves, particularly those of the abdominal viscera. Clinically, it is known that abnormalities in the gastric motor mechanism may occur during periods of emotional disturbances. Many investigators¹² have reported that under such circumstances gastric motility is inhibited. Similar results have been reported by Ivy,^{10a} Carlson² and others.¹³ On the other hand, there are several investigators who maintain that hypermotility is the most common observation.¹⁴ There is consequently a lack of uniformity in the composite results reported in the literature.

Since it was possible to study gastric motility in patients who were experiencing the emotional disturbance which usually precedes a major operation, kymographic tracings were made for periods of about three hours preceding herniorrhaphy and were continued until the patients were taken to the operating room. It was our experience that gastric hypermotility was the most common observation under these circumstances. In many instances the contractions were severe, although the duration of the periods of gastric activity was not unusually prolonged. By means of the electric key and the signal magnet it was possible to observe that epigastric distress occurred during periods of intense motility.

We cannot conclude from our own findings or from the reports of other investigators that either hypermotility or inhibition necessarily occurs during emotional states. It is possible that either may appear,

11. Carlson, A. J., and Litt, S.: Studies on the Visceral Nervous System: On the Reflex Control of the Pylorus, *Arch. Int. Med.* **33**:281 (March) 1924.

12. Cannon, W. B.: The Movements of the Stomach Studied by Means of the Röntgen Rays, *Am. J. Physiol.* **1**:359, 1898. Todd, T. Wingate: *Behavior Patterns of the Alimentary Tract*, Baltimore, Williams & Wilkins Company, 1930.

13. Luckhardt, Arno B.: The Effect of Dreaming on the Gastric Hunger Contractions, *Am. J. Physiol.* **39**:330, 1915-1916.

14. Barber.⁴ Hughson.^{9b}

depending on the preexisting tonus of the stomach and the type of emotional distress manifested. This problem is complex and doubtless is influenced by a multiplicity of factors, which are neither constant nor uniform throughout the studies made by various investigators—hence the discrepancies.

Although it was our experience to observe hypermotility during the emotional changes preceding operation, it is impossible to conclude that it will uniformly occur until emotions are more clearly defined and more accurately investigated.

Motor inhibition of the gastro-intestinal tract is frequently encountered during abdominal laparotomy. This phenomenon was described by Pal as early as 1890.¹⁵ Since then it has been reported by many investigators. Bayliss and Starling¹⁶ found that when the abdomen of a dog was opened in a warm bath of saline solution the intestines were collapsed and motionless. Section of the splanchnic nerves or even radical destruction of the spinal cord was necessary to institute intestinal motility. Similarly, Meltzer and Auer¹⁷ reported that merely cutting the skin in the linea alba of a rabbit was sufficient to abolish peristalsis of the cecum. Auer¹⁸ observed that opening the abdominal cavity of the rabbit caused cessation of gastric movements. Our studies on the human stomach are in agreement with these experimental observations.

We observed inhibition of the gastric motility during herniorrhaphy. This persisted for a varying period, of from twenty-four to approximately seventy-two hours, postoperatively. It would seem that this temporary gastric paresis was due to reflex stimulation of the splanchnic nerves and due to a mechanism similar to that described by Markowitz and Campbell¹⁹ and Ochsner, Gage and Cutting²⁰ for the production of physiologic ileus. Our tracings show that the motility eventually returned and that hypermotility subsequently ensued.

During this postoperative period of temporary inhibition of gastric motility or physiologic paralysis of the stomach, gastric distention was most evident. It is possible that this distention, if sufficiently extensive.

15. Pal, J.: Ueber den Einfluss des Bauchschnittes auf die Darmbewegung. *Centralbl. f. Physiol.* 4:338, 1890.

16. Bayliss, W. M., and Starling, E. H.: The Movements and Innervation of the Small Intestine, *J. Physiol.* 24:99, 1899.

17. Meltzer, S. J., and Auer, J.: Peristaltic Movements of the Rabbit's Cecum and Their Inhibition, *Proc. Soc. Exper. Biol. & Med.* 4:37, 1907.

18. Auer, John: Gastric Peristalsis Under Normal and Certain Experimental Conditions, *Proc. Soc. Exper. Biol. & Med.* 4:8, 1907.

19. Markowitz, J., and Campbell, Walter R.: The Relief of Experimental Ileus by Spinal Anesthesia, *Am. J. Physiol.* 81:101, 1927.

20. Ochsner, Alton; Gage, I. M., and Cutting, R. A.: Treatment of Ileus by Splanchnic Anesthesia, *J. A. M. A.* 90:1847 (June 9) 1928.

acts as a stimulus to the gastric motor mechanism so that hypermotility follows. In 1904 May²¹ reported that hypermotility occurred when the dog's excised stomach was inflated with air. Lim, Ivy and McCarthy²² made similar observations. They found that when over-distention occurred there ensued a decrease in motility and in tone. It would seem from our observations that the distention occurring during this physiologic adynamic period increased until it reached the maximal threshold level peculiar to each patient. The ensuing hypermotility was then probably the result of mechanical stimulation to the gastric motor mechanism in a manner similar to that previously reported. This post-operative hypermotility persisted for from ten days to two weeks. Occasionally it was seen throughout the entire period of postoperative convalescence. In other instances it returned to normal prior to the patient's discharge from the hospital.

It is probable that reflex stimulation of the gastric sensory mechanism occurs simultaneously with the hypermotility of the stomach. The most common subjective sensation experienced by the patients during the early postoperative period of increased gastric activity was a form of epigastric distress interpreted by them as gas pains. These were intermittent and coincided with the severe contractions. Subsequently the patients complained of intense hunger as a late manifestation of increased gastric activity.

Although the early postoperative epigastric distress was interpreted as gas pains and although this occurred during a period of intense gastric activity, we do not think that the hypermotility alone is responsible for this sensation. Obviously there are other factors intimately involved in this problem. Nevertheless, there was sufficient evidence to indicate that in the genesis of postoperative epigastric distress the gastric motor mechanism assumed an important rôle. We would think that inhibition of the gastric motility followed by the hypermotility has certain clinical implications which are significant in understanding the nature of early postoperative disturbances.

The spinal anesthesia which was used during the repair of the hernias did not extend beyond the operative field. The work of other investigators²³ reveals that hypermotility of the gastro-intestinal tract ensues only if the spinal anesthesia produces paralysis of the splanchnic nerves. We observed no evidence that this occurred during our studies.

21. May, W. Page: The Innervation of the Sphincters and Musculature of the Stomach, *J. Physiol.* **31**:260, 1904.

22. Lim, Robert K. S.; Ivy, A. C., and McCarthy, J. E.: Contributions to the Physiology of Gastric Secretion: I. Gastric Secretion by Local (Mechanical and Chemical) Stimulation, *Quart. J. Exper. Physiol.* **15**:13, 1925.

23. Markowitz and Campbell,¹⁰ Ochsner, Gage and Cutting.²⁰

Although we cannot outline with certainty the physiologic mechanism responsible for the production of this inhibition during laparotomy and for a varying period subsequently, we do not think that spinal anesthesia *per se* is the cause. The work of Markowitz and Campbell¹⁹ and Ochsner, Gage and Cutting²⁰ would lead us to believe that spinal anesthesia is responsible for hypermotility as a result of paralysis of the splanchnic nerves. This hypermotility occurred after an extremely short latent period.

The hypermotility evident on our tracings appeared from one to three days subsequent to operation. Therefore, it is our belief that the mechanism which is responsible for the inhibition of gastric motility which we observed during operation and for a varying period subsequently is similar to the mechanism which is responsible for the inhibition of the intestinal motility during laparotomy, a phenomenon already described.¹⁹ The hypermotility which followed might possibly be due to stimulation of the gastric motor mechanism by the mechanical distention of the stomach occurring during the period of inhibition.

CONCLUSIONS

Gastric motility was studied by the balloon and kymograph method on seven patients on whom laparotomy was performed. The results of this investigation revealed the following facts:

1. There was a tendency toward hypermotility of the stomach in patients with untreated cholecystitis associated with cholelithiasis.
2. Continuous gastric motility was associated with occasional severe contractions during biliary colic.
3. Increased gastric hypermotility persisted for from two to three weeks after cholecystectomy. During the first week of this increased motility the patients experienced epigastric distress interpreted by them as gas pain; subsequently they complained of intense hunger as a late manifestation of hypermotility.
4. Normal gastric motility was present in five patients with inguinal hernia until immediately preceding hernial repair, at which time short but intense periods of gastric activity, associated with emotional disturbance, were observed.
5. Inhibition of gastric motility persisted throughout herniorrhaphy and for from twenty-four to seventy-two hours subsequently.
6. Gastric hypermotility subsequent to inhibition persisted for from two to three weeks, during which the subjective sensations were similar to those described after cholecystectomy.

CARCINOMA OF THE FEMALE BREAST

WITH SPECIAL CONSIDERATION OF PREOPERATIVE IRRADIATION:
A PRELIMINARY REPORT

L. CLARENCE COHN, M.D.

BALTIMORE

In the recent surgical literature there are seven articles to which I should like to call special attention.¹ Six of these deal with preoperative irradiation in the treatment of carcinoma of the breast. The seventh is concerned chiefly with the statistical study of cancers of the breast treated by surgical measures alone and by surgical measures and post-operative irradiation. From one of these articles, namely, that of Adair and Stewart, I have taken the following data on eighty-one cases of operable carcinoma of the breast in which preoperative irradiation was followed by a radical Halstead operation.

Radium element pack.....	39 cases
No residual cancer.....	11 cases (28%)
Roentgen therapy, 200 kilovolts.....	42 cases
No residual cancer.....	7 cases (16%)

In each of these cases biopsy was performed preliminary to irradiation.

In the *Nova Scotia Medical Bulletin* of June 1935 Bloodgood gave his conclusions in favor of irradiation preliminary to operation for carcinoma of the breast.

Bloodgood and Stewart, in a brief paper in the *Southern Medical Journal* for July 1936, made further remarks on the preoperative irradiation of cancer of the breast and reported a case which I shall refer to again in this article.

From the clinic of the late Dr. Joseph C. Bloodgood and his associates.

1. Bloodgood, Joseph Colt: The Problem of the Breast Tumor, *Nova Scotia M. Bull.* **14**:307 (June) 1935. Cohn, L. Clarence: Benign Breast Lesions, with Special Consideration of Border-Line Tumors: Cancer of the Breast and the Newer Conception of Preoperative Irradiation, *West Virginia M. J.* **31**:1 (Jan.) 1936. Adair, Frank E., and Stewart, Fred W.: The Value of Preoperative Irradiation in Breast Cancer, *Ann. Surg.* **102**:254 (Aug.) 1935. Hutchinson, R. G.: The Value of Radiation Therapy in the Treatment of Carcinoma of the Breast, *Surg., Gynec. & Obst.* **62**:653 (April) 1936. Nicolson, W. P., and Berman, M. D.: Carcinoma of the Breast: A Study of Five Year End-Results, *Ann. Surg.* **103**:683 (May) 1936. Graham, Allen: Cancer of the Breast, with Particular Reference to Irradiation as a Factor in End-Results, *Pennsylvania M. J.* **39**:561 (May) 1936. Bloodgood, Joseph Colt, and Stewart, G. A.: Preoperative Irradiation of Breast Tumors, *South. M. J.* **29**:651 (July) 1936.

My first experience with the preoperative irradiation of operable cancer of the breast was in 1927, almost ten years ago, and was what might be described as an accident. This concerned a married woman aged 42, whose youngest child was 9 years of age.

I examined the patient with Dr. Bloodgood on March 28, 1927, and we found a gland the size of a 5 cent piece in the base of the right axilla, with a smaller definite nodule in the periphery of the right breast just adjoining the gland. She had felt the lump only four days. Although the roentgenogram of the chest was normal, we decided to use irradiation for the first treatment because of the possibility of lymphosarcoma. When I examined her on May 2, more than four weeks later, and two weeks after roentgen therapy (200 kilovolts), the lump had decreased in size two-thirds and was smaller than a 10 cent piece. As the nodule did not disappear, I decided to do a complete axillary dissection. I made the usual axillary incision as in the complete operation for cancer of the breast, divided the pectoralis major and minor muscles, exposed the axillary vein and dissected the axilla from above downward. On introducing the finger beneath the palpable tumor, finding that the tumor felt like cancer and that it would be necessary to remove a considerable portion of the breast to give the tumor the proper margin, I decided on the usual complete operation for cancer of the breast, doing the dissection of the wall of the chest after the axillary dissection—the reverse of our usual method. In doing the axillary dissection I was unable to palpate any glands except this nodule in the base of the axilla, which had been palpated prior to the operation.

The frozen section showed a cellular medullary carcinoma, and there was no metastasis to the axillary glands.

The patient is now (September 1936) well, almost ten years after operation. This tumor must be looked on as carcinoma in the axillary quadrant of the breast or as carcinoma in aberrant breast tissue in the axilla.

On April 28, 1930, more than three years later, a widow 35 years of age consulted Dr. Bloodgood with a microscopic section from a carcinoma excised from the left breast on Dec. 9, 1929, four and a half months previously. The tumor had been present only one month before it was excised, and it was clinically benign. At the examination Dr. Bloodgood was unable to palpate any nodules in the scar, breast or axilla. He decided to give irradiation, which was carried out from April 28 to May 9.

Dr. Bloodgood decided on irradiation first because he felt that the chief danger was that metastasis had already taken place during the four and one-half month interval since the operation. When the patient returned on October 13, five months later, examination of the breast gave entirely negative results, but a second course of irradiation was given over the breast, axilla and mediastinum. There has been no further operation other than the excision of the tumor, and the patient is now well, six and a half years since the operation.

On Dec. 12, 1931, Mrs. T. consulted us with an operable but very advanced carcinoma of the breast in which there was beginning carcinoma *en cuirasse* (fig. 1 A). Figure 1 B shows the result three months after irradiation, and the patient is now well, five years after treatment. The only treatment was one course of irradiation. No biopsy was done in this case; so the only evidence that this patient had cancer was clinical.

Preoperative irradiation was not taken up seriously in this clinic until the summer of 1932, four years ago, when Dr. Bloodgood returned

from a visit to some of the outstanding radiologic clinics in Europe. At that time I was much opposed to giving a patient with carcinoma of the breast preoperative irradiation and felt that there was a distinct danger in delaying the operation for irradiation, and I believe this is the view of the majority of my colleagues today.

On June 15, 1932, more than four years ago, Mrs. M. J., aged 57, consulted us because of a large, visible mass occupying the entire right breast, producing a dome-shaped bulging of the breast with the nipple at the top of the dome. The mass was adherent to the skin and the nipple, and there was fixation of the nipple and of the areola. In spite of the extensive involvement of the breast, there were no palpable glands in the axilla. The tumor had been present for five months. The patient was referred to the Kelly Hospital for preoperative irradiation. This was carried out by Dr. Edmond Kelly, from whose notes the following information was taken: During June 1932 a total of 8 gram hours of radium treatment was given at a distance of 5 cm. directly to the right axilla with the pack; also



Fig. 1.—*A*, photograph of a patient taken on Dec. 12, 1931, showing an advanced, clinically malignant tumor of the breast. *B*, the same patient on March 23, 1932, after treatment by irradiation only. The patient was still well in May 1936.

5 gram hours at a distance of 4 cm. to the right lateral aspect of the right breast and similar treatment to the left lateral aspect of the right breast. In addition to this, nine 4.2 millicurie gold needles were implanted permanently into the substance of the breast, scattered equally through its periphery, yielding a total radiation of approximately 4.5 gram hours during the life of the needles (twenty-eight days). The patient was then given 5 gram hours at a distance of 4 cm. to the right supraclavicular space. In addition, she was given high voltage roentgen therapy through a portal 10 by 10 cm., 900 roentgens each to the anterior and the posterior surface of the right axilla.

The total amount of radiation was given in ten days and was completed on June 25. On September 30, more than three months later, Dr. Bloodgood and I did the operation, which consisted of an exploratory incision (definite cancer was observed in the frozen sections) and the excision of the breast and pectoral muscles but not of the axilla. The axillary dissection was omitted because of the precarious condition of the patient. Figure 2 shows the appearance of the patient before and after operation, and figure 3, the microscopic pathologic picture. The

patient is now well more than four years after operation and is our first example of a patient with an operable but advanced carcinoma of the breast who was cured for four years by complete irradiation and incomplete surgical excision.

Later I shall give the figures on excision of the breast only (including dissection of the wall of the chest) with and without preoperative irradiation. The total number of patients in this group is small, and the therapy is not, in my opinion, the treatment of choice. The foregoing case marked the beginning of our intensive study of preoperative irradiation for carcinoma of the breast.

DATA ON CASES OF PRIMARY AND RECURRENT CARCINOMA OF THE BREAST

For the purposes of the present study all cases of primary and recurrent carcinoma of the breast observed in the clinic from January



Fig. 2.—*A*, photograph of a patient with a cancer involving the larger part of the breast. *B*, the same patient after operation. (These photographs were previously published by Bloodgood, J. C.: *Am. J. Surg.* 28:490, 1935.)

1931 to December 1935 are included, or, in other words, during the immediate preceding five year period, and while it is clear that any report on such a recent series of cases may be criticized as premature, it was felt that a preliminary report at this time might bring out and emphasize what seems to be the keynote of the problem, which is that there is apparently no danger in delaying the complete operation for one course of preoperative irradiation.

A summary of the data to be analyzed is presented in table 1, and while it is realized that the number of patients studied is not large, the numbers in the different groups seem to be near enough equal so as to allow some basis for comparison, and I plan to report on the same series again at the end of five years.

At this writing (September 1936) from four years to nine months has elapsed since therapy in the cases in which irradiation was employed, with one exception, and in the cases in which surgical treatment only was used from two to five years or more has elapsed.

In table 1, the patients in groups 1, 2 and 3 include the majority of those with primary carcinoma, and it is these patients who attract particular attention. When one compares the data in table 2 with those

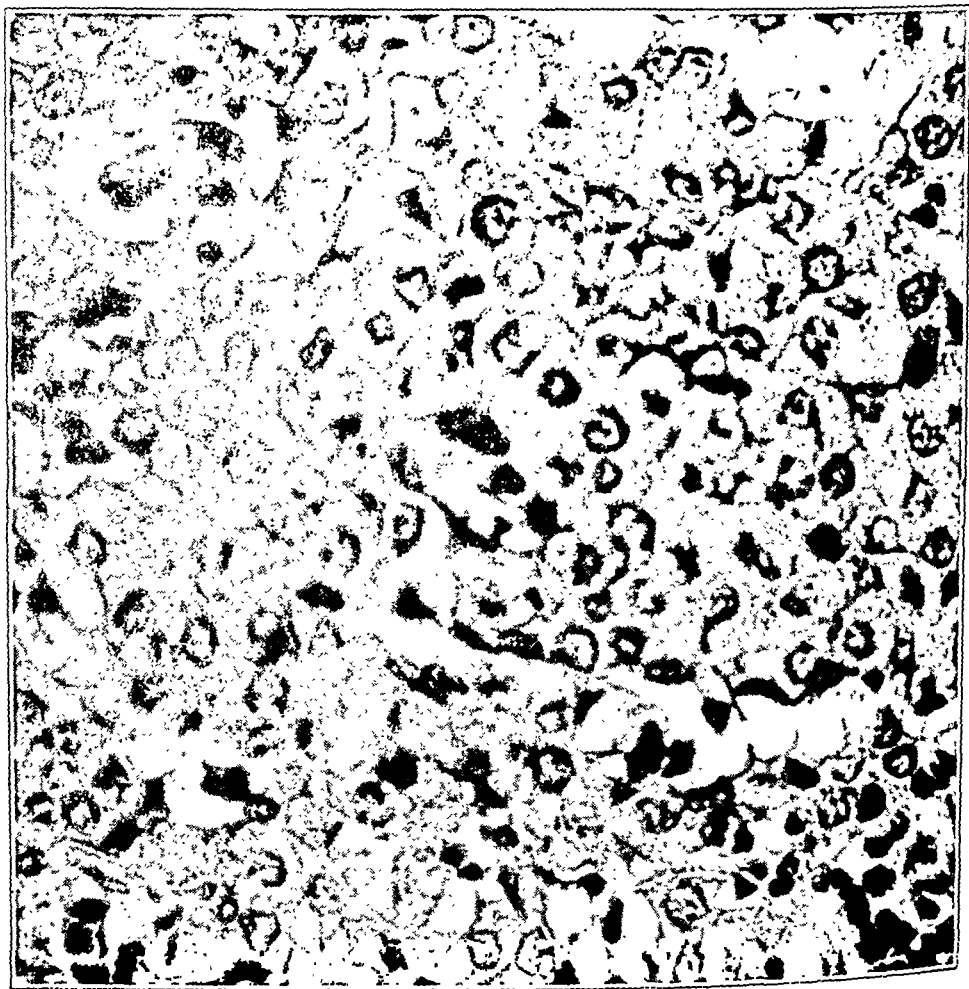


Fig. 3.—Photomicrograph of the tumor shown in figure 2A.

in table 3 one is comparing the results in forty-three patients who were subjected to preoperative irradiation followed by the complete operation with those in fifty-one patients who underwent complete operation without preoperative irradiation. Of the former group, thirty, or 71 per cent, are living and free from recurrence, while of the latter group, only seventeen, or 33 per cent, are living and free from recurrence. While eight of the former group died of cancer and four are living with recur-

rence (28 per cent), twenty-eight of the latter group are dead of cancer and three are living with recurrence (60 per cent).

However, for the group of thirty patients living and free from recurrence after preoperative irradiation followed by the complete operation the average length of time since irradiation was begun is only one year and ten months, whereas for the group of seventeen patients living and free from recurrence after the complete operation only the average length of time since operation is three years and four months. For the group of twelve patients dead or living with recurrence after preoperative irradiation plus the complete operation, the average length of time since irradiation was begun is one year and nine months, and for the group of thirty-one patients dead or living with recurrence after the complete operation only, the average length of time since operation is one year and seven months.

TABLE 1.—*Classification of Patients According to Treatment and Results*

Group	Status	No. of Patients
1	Preoperative irradiation and complete operation.....	43
2	Complete operation; no preoperative irradiation.....	51
3	Irradiation only, including excision of tumor and biopsy.....	42
4	Excision of breast only.....	9
5	Recurrent carcinoma.....	41
6	Insufficient record.....	6
Total.....		192

If such limited statistics indicate anything, it is interesting to note that there is apparently no evidence that the addition of preoperative irradiation prolongs the duration of life in those persons who are to die of the disease.

It should again be emphasized at this point that the figures and percentages given in tables 2 and 3 and in the subsequent tables are merely the figures and percentages as they have been worked out for the present study and should not be interpreted except in this light. They are not given as proof or even as arguments in favor of preoperative irradiation or that preoperative irradiation followed by the complete operation will cure, for five years or longer, a larger percentage of patients. The solution of this problem, at least as far as this series of patients is concerned, will have to await the passage of time. On the other hand, the reason for the publication of these figures is that sufficient time seems to have elapsed to indicate that there is apparently no danger in delaying the complete operation for one course of preoperative irradiation, provided sufficient time elapses between the irradiation and the operation, and in our experience the optimum time for the operation is from two and a half to three months after the irradiation is completed. This interval allows the skin and deeper struc-

tures to return to normal, even though there have been blistering and epitheliitis from the irradiation.

At the beginning we were inclined to operate too soon after completion of the irradiation. The only death occurred in the following case:

The patient consulted us on May 10, 1934, with a section from a tumor which had been removed from her breast six days previously. The section showed medul-

TABLE 2.—*End-Results for Patients in Group 1*

Total number of patients.....	43
Living, free from recurrence.....	30 (71%)
Death from cancer.....	8 } (28%)
Living with recurrence.....	4 }
Death postoperatively, due to infection.....	1 }
Average length of time since irradiation was begun for patients living and free from recurrence.....	1 yr., 10 mo.
Average length of time since irradiation was begun for patients dead or living with recurrence.....	1 yr., 9 mo.

TABLE 3.—*End-Results for Patients in Group 2*

Total number of patients.....	51
Living, free from recurrence.....	17 (33%)
Death from cancer.....	28 } (60%)
Living with recurrence.....	3 }
No note.....	2 }
Death from another cause.....	1 }
Average length of time since operation for patients living and free from recurrence.....	3 yr., 4 mo.
Average duration of life after operation for patients dead or living with recurrence.....	1 yr., 7 mo.

TABLE 4.—*End-Results for Patients in Group 3*

Total number of patients.....	42
Living and well.....	13 (31%)
Death from cancer.....	26 (62%)
Lost from observation.....	2 } (7%)
Death from another cause.....	1 }
Average duration of life from onset of tumor (from history) until death.....	23 mo.
Average duration of life from time of admission (irradiation) until death.....	14 mo.
Average length of time since admission (irradiation) for patients living and well.....	2 yr., 3 mo.
Average length of time since onset of disease for patients living and well.....	2 yr., 8 mo.

lary carcinoma, and there was a small gland palpable in the axilla. She was given a course of preoperative irradiation from May 10 to May 26. When she returned on July 10, less than two months later, there was a small nodule in the upper end of the scar of two weeks' duration, and for this reason we decided on a second course of irradiation before operating. The second course was begun on July 10 and was completed on July 20, at which time the little nodule that we had felt in the scar ten days previously had entirely disappeared, and the little gland that we had palpated in the axilla on May 10 was no longer palpable. When the patient returned for her next examination, on October 22, there was no evidence of any

recurrence of the disease in the breast or the axilla. Three months later, at our examination on Jan. 25, 1935, there was another nodule in the scar of one month's duration, and a third course of irradiation was given, from January 25 to February 12. On February 15, three days later, I did the complete operation. Sections from the breast and axilla showed no residual cancer. Dr. Gey reported the tissue culture to be negative.

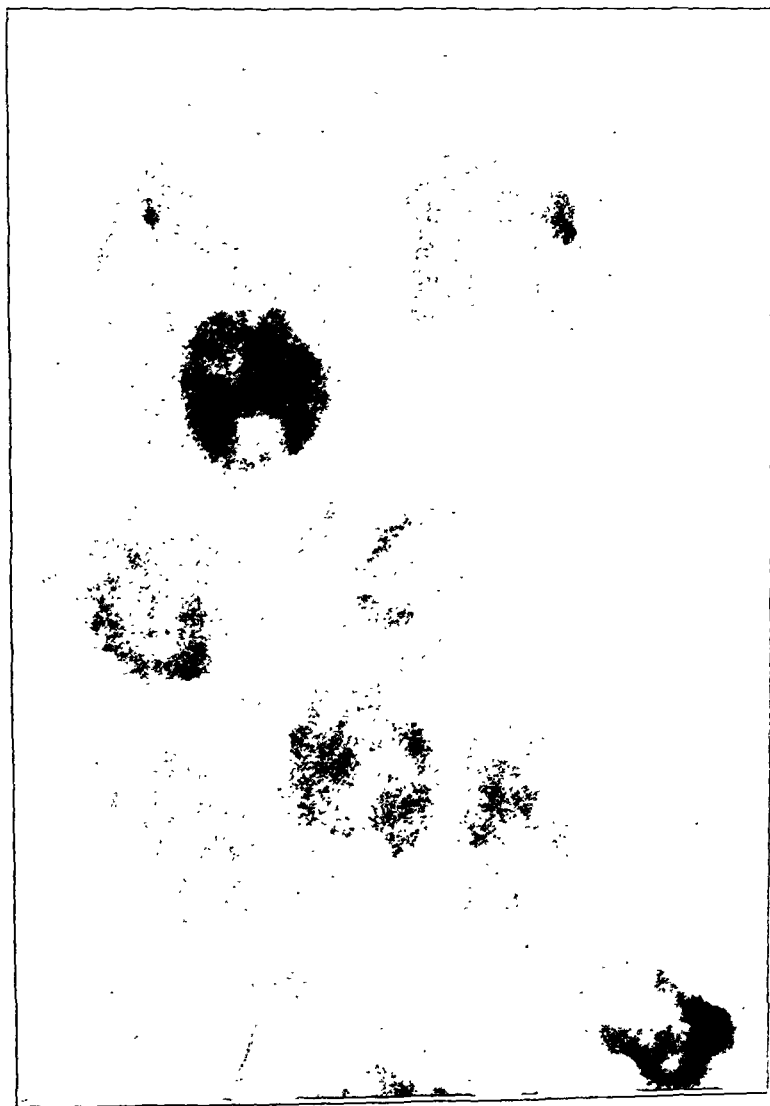


Fig. 4.—High power photomicrograph of a smear made from a biopsy specimen secured by aspiration, showing cells distinctly of the malignant type. (This photograph was previously published by Bloodgood, J. C., and Stewart, G. A.: *South. M. J.* 29:651, 1936.)

The wound became infected with hemolytic streptococci, and in spite of our recognizing the infection at once and starting treatment with diluted solution of sodium hypochlorite, the patient died on the tenth day after operation. This is the only infection due to hemolytic streptococci that we have had in a breast wound since the influenza epidemic in 1918, and it is quite possible that it was an accidental occurrence, but I have always felt that the tissues were unable to take care of this infection because they had not yet recovered from the injury of the irradiation.

Of the forty-three patients on whom preoperative irradiation and the complete operation were done, twenty-eight received irradiation without a biopsy because the tumor was clinically malignant, and one patient

TABLE 5.—*Data Concerning Biopsy and Tissue Culture on Patients in Group 1*

Total number of patients.....	43
Biopsy	16
Before irradiation	15
Excision of tumor	14
Aspiration	1
After irradiation—followed by complete operation.....	1
No biopsy	27
Tissue cultures made.....	23
Positive	6 (29%)
Negative	15 (71%)
Questionable	2
No cultures made.....	20

TABLE 6.—*Data Concerning Tissue Culture on Patients in Group 2*

Total number of patients.....	51
Tissue culture positive.....	2
Tissue culture negative.....	2
No culture taken.....	47
Postoperative irradiation as a routine.....	9
Postoperative irradiation after recurrence.....	10

was treated with irradiation followed by a biopsy and immediately after the biopsy by the complete operation. Biopsy was done for fifteen patients before irradiation, excision of the tumor being done in fourteen instances and aspiration in one instance (fig. 4). Tissue cultures were taken in twenty-three of the forty-three cases and were reported by Dr. Gey as positive in six instances (29 per cent) and negative in fifteen instances (71 per cent). The tissue culture was questionable in two cases (table 5). What the significance of the growth of the tumor or the lack of the growth of the tumor in tissue culture is as yet is not known because in the fifty-one cases in which the complete operation was done without preoperative irradiation the tissue culture was taken in only four instances. It was positive twice and negative twice (table 6).

In connection with biopsy, there is one case I shall report a little more in detail because the procedure followed was so unorthodox and brings up the question of what shall be done for a clinically benign tumor which in a frozen section proves to be cancer.

On Nov. 5, 1935, I explored a clinically benign tumor, smaller than a 25 cent piece, of two months' duration, in a woman 46 years of age. After excising the tumor and bisecting it, I was convinced that it was carcinoma, and immediate preparation and study of a frozen section confirmed this. The gross and microscopic pictures are presented in figures 5 and 6. In this case, instead of disinfecting the wound and doing the complete operation, I simply closed the wound and referred the patient to Dr. Neill for irradiation, which was started at once to the supra-clavicular area and axilla; after about one week, during which time the wound in the breast healed, the irradiation was carried over the breast. Figure 7 is the photograph of the patient after irradiation.



Fig. 5.—Photograph of the gross specimen of a clinically benign tumor.

On Jan. 21, 1936, three months later, I did the complete operation (fig. 8). There was no metastasis to the axillary glands, and there was no residual carcinoma in the breast. A culture of tissue from the tumor was positive, and one was also reported to be positive after the complete operation.

The chances of curing a patient with a tumor like this for five years by surgical measures alone are 70 per cent, and it remains to be seen whether the addition of this preoperative irradiation will increase or decrease the chances of a cure.

Of the forty-three patients subjected to preoperative irradiation and the complete operation, we found no residual cancer in the breast or axilla in ten (24 per cent), and of these ten, biopsy was performed for seven. We found residual cancer in the breast or axilla of thirty-two patients (76 per cent), as shown in table 7. These figures should be compared with those of Adair and Stewart.

The factors which seem to influence the prognosis are the grade of malignancy of the tumor (Broders), the presence or absence of glandular involvement and the extent of the involvement. The grade of the tumor is really an index of the rapidity of the growth, whereas the involvement of the axillary glands is an index of the extent of the growth and depends to some extent on the grade, but perhaps more on the duration of the tumor. I shall take up the question of involvement

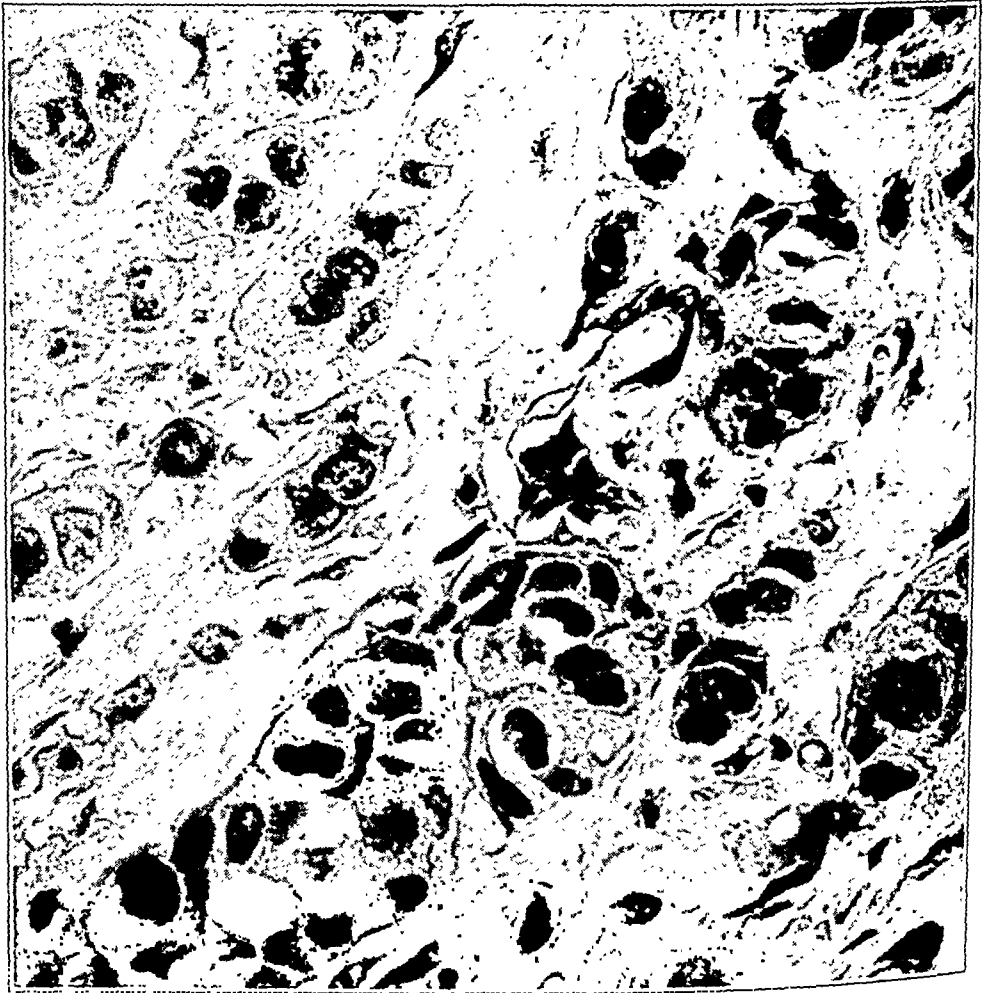


Fig. 6.—Photomicrograph of a clinically benign tumor.

of the glands first (tables 8 and 9). Of the group of forty-three patients on whom preoperative irradiation and the complete operation were done, the glands were involved in eighteen (44 per cent) and showed no metastasis in twenty-three (56 per cent). Of the group with no metastasis to the axillary glands, twenty-one are well (91 per cent), one died of cancer and one died of some other cause. Of the eighteen patients in whom the glands were involved, eight (44 per cent) are well and ten (56 per cent) died of cancer (table 8).

Of the group of fifty-one patients subjected to the complete operation but without preoperative irradiation, there was no metastasis to the axillary glands in fourteen (30 per cent).



Fig. 7.—Photograph of a patient after excision of the tumor and irradiation. For the gross and microscopic appearance of the tumor see figures 5 and 6.

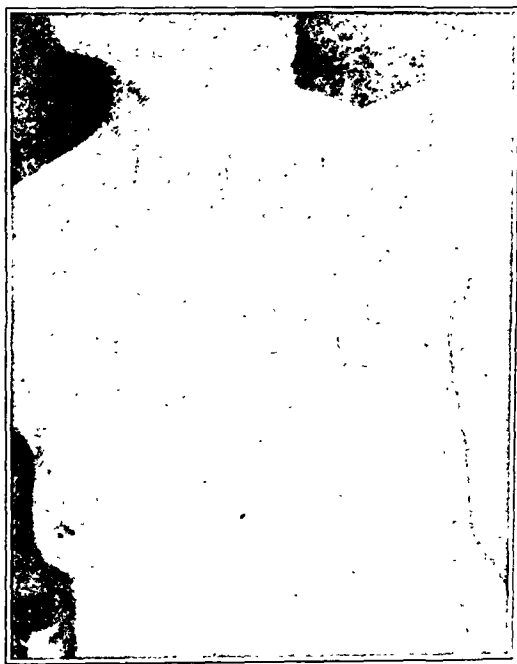


Fig. 8.—Photograph of the patient shown in figure 7 after complete operation.

Frequently I have been able to palpate axillary glands prior to irradiation and three months later prior to operation all evidence of

palpable axillary glands had disappeared; it seems quite possible that the irradiation is responsible for the higher percentage of patients free from axillary involvement—56 per cent in the group treated by irradiation as compared with 30 per cent in the group on whom irradiation was not done. From tables 8 and 9, it is seen that 91 per cent of the patients who were free from involvement of the glands were well after preoperative irradiation and the complete operation and that 90 per cent of those without metastasis to the glands were well after complete

TABLE 7.—*Data Concerning Residual Cancer in Patients in Group 1*

Total number of patients.....	43
No residual cancer in breast or axilla.....	10 (24%)
Biopsy, consisting of excision of tumor.....	7
No biopsy	2
Sections unsatisfactory	1
Residual cancer in breast or axilla....	32 (76%)
No note	1

TABLE 8.—*End-Results in Relation to Metastasis in Patients in Group 1*

Total number of patients.....	43
No metastases to glands.....	23 (56%)
Well	21 (91%)
Death from cancer.....	1
Death from another cause.....	1
Metastases to glands.....	18 (44%)
Well	8 (44%)
Death from cancer.....	10 (56%)
No note	2

TABLE 9.—*End-Results in Relation to Metastasis in Patients in Group 2*

Total number of patients.....	51
No metastasis to glands.....	14 (30%)
Well	9 (90%)
Death from cancer.....	1 (10%)
Death from another cause.....	1
No record	3
Metastasis to glands.....	33 (70%)
Well	8 (24%)
Death from cancer.....	25 (76%)
No note	4

operation only; so there is no evidence yet that irradiation is of value in early cases of cancer in which there is no involvement of the axillary glands, but there is no evidence that it is harmful, even though it may be unnecessary. On the other hand, 44 per cent of the patients with metastasis to the glands who were subjected to preoperative irradiation plus complete operation were well, as compared with 24 per cent of those who were treated with complete operation alone. It is to be emphasized, however, that the patients who received irradiation on the average have been treated more recently than those who were not treated by irradiation.

When only the glands at the base of the axilla are involved, the complete operation alone offers about 25 per cent chances of a five year cure. In the cases included in this report, which I have already stated is not a report of five year cures, there were seven patients on whom the complete operation without preliminary irradiation was done in whom only the glands of the base of the axilla showed metastasis, and of these seven only two are well (29 per cent) and five are dead of cancer (71 per cent). In the group on whom preoperative irradiation plus the complete operation was done, there are six in whom only the

TABLE 10.—*End-Results in Relation to Extent of Metastasis in Patients in Group 1*

Total number of patients.....	43
Glands plus	15 (44%)
Well	8 (44%)
Death from cancer.....	10 (56%)
Gland 1 plus.....	6
Well	4 (66.66%)
Death from cancer.....	2 (33.33%)
Glands 1, 2 plus.....	1 well
Glands 1, 2, 3 plus.....	5
Well	1 (12.5%)
Death from cancer.....	7 (88.5%)

TABLE 11.—*End-Results in Relation to Extent of Metastasis in Patients in Group 2*

Total number of patients.....	51
Glands plus	33 (70%)
Well	8 (24%)
Death from cancer.....	25 (76%)
Glands 1 plus.....	7
Well	2 (29%)
Dead	5 (71%)
Glands 1, 2 plus.....	6
Well	1 (17%)
Death from cancer.....	5 (83%)
Glands 1, 2, 3 plus.....	12
Well	2 (17%)
Death from cancer.....	10 (83%)

glands of the base of the axilla showed metastasis, and of these, four (66.6 per cent) are well. The actual number of patients with involvement of the glands of the base and the middle of the axilla or of the base, the middle and the highest apex of the axilla is greater in the group who did not receive irradiation, but the number of patients in each group is too small to allow any conclusions (tables 10 and 11).

Tables 12 and 13 are compiled to show the ultimate result according to the microscopic grading of the tumor in the forty-three patients on whom preoperative irradiation and the complete operation were done and in the fifty-one on whom the complete operation was performed but no preoperative irradiation was given. Of the patients in the first group, 75 per cent with a tumor of grade 1 or grade 2 are well and

25 per cent died of cancer, whereas of those in the second group, 70 per cent are well and 30 per cent died of cancer, an insignificant difference in the percentages. Sixty-one per cent of the patients with tumors of grade 3 who were given irradiation are well, as against 23 per cent of the patients with this grade of tumor who were not given irradiation. The number of patients with a tumor of grade 4 in both groups is too small to be of any value in this study. From these figures it would seem that if there is any value in preoperative irradiation it is for the tumor of grade 3.

TABLE 12.—*End-Results in Patients in Group 1 in Relation to Grade of Tumor*

Total number of patients.....		43
Grade 1 tumor.....		48
Well	6 (75%)	
Death from cancer.....	2 (25%)	
Grade 2 tumor.....		12
Well	9 (75%)	
Death from cancer.....	3 (25%)	
Grade 3 tumor.....		18
Well	11 (61%)	
Death from cancer.....	7 (39%)	
Grade 4 tumor.....		2
Well	1	
Death from another cause.....	1	
No residual cancer.....		2
Sections unsatisfactory		1

TABLE 13.—*End-Results in Patients in Group 2 in Relation to Grade of Tumor*

Total number of patients.....		51
Grade 1 tumor.....		None
Grade 2 tumor.....		13
Well	7 (70%)	
Death from cancer.....	3 (30%)	
Death from another cause.....	1	
No note	2	
Grade 3 tumor.....		27
Well	6 (23%)	
Death from cancer.....	20 (77%)	
No note	1	
Grade 4 tumor.....		2
Well	1 (50%)	
Death from cancer.....	1 (50%)	
No note		9

In this series of one hundred and ninety-two patients it has already been noted that there were forty-two with primary carcinoma on whom irradiation only or excision of the tumor or some other type of biopsy plus irradiation was performed (table 4). Up to the present time irradiation has not been advised as the only treatment in any case of primary operable carcinoma of the breast except to a few patients over 70 years of age in whom the tumor was arrested by irradiation and to two younger women with acute carcinoma, and in these all evidence of the tumor in the breast and axillary glands disappeared rapidly under irradiation.

Of this group of forty-two patients, thirteen had clinically operable tumors. Two of these were the young women with acute carcinomas, and the remaining eleven were older women. There were a few patients in this group who refused the complete operation. Of the thirteen with operable tumors who were given irradiation only, 66 per cent are well (table 14). As the tumor and axillary glands disappeared so rapidly under irradiation in the two patients with acute carcinoma, we decided not to operate because we felt that the chief danger was distant metastases and that should the tumor recur in the breast or axillary glands we could always operate. These patients were kept under constant observation. One of the patients died of cancer one year and eight months after the beginning of irradiation, but there was no recurrence in the

TABLE 14.—*End-Results in Patients in Group 3*

Total number of patients.....	42
No biopsy	29
Biopsy	13
Excision of tumor.....	8
Clinically operable tumors.....	13
Well	8 (66%)
Average duration of time since admission (irradiation).....	2 yr., 3 mo.
Death from cancer.....	4 (33%)
Average duration of life after irradiation	1 yr., 8 mo.

TABLE 15.—*End-Results in Patients Subjected to Excision of the Breast Only*

Total number of patients.....	9
No recurrence	4
Average duration of time since operation.....	3 yr., 3 mo.
Death from cancer.....	4
Average duration of life since operation.....	2 yr.
Death from other cause.....	1
Duration of life after operation (no recurrence).....	2 yr., 11 mo.

breast or axilla until two months before death, at which time she was bedridden because of metastases to the pelvis, lower lumbar vertebrae and chest. The other patient is well and free from clinical evidence of cancer one year and two months after irradiation began, during which period there have been two courses of irradiation.

The other twenty-nine patients who received irradiation only had clinically inoperable tumors, so there was no choice in treatment other than irradiation. It has already been noted in table 4 that 31 per cent of these patients are well and that the average period of time since irradiation was begun is two years and three months.

One of the reasons for publishing this material at this time as a preliminary report is that there is such a great difference of opinion between radiologists of experience and surgeons of experience. Some radiologists feel that carcinoma of the breast is no longer a surgical problem and that the treatment should be left entirely to the radiolo-

gists. They strongly object to the complete operation but occasionally agree to a simple mastectomy. On the other hand, the majority of surgeons of experience have not accepted as yet preoperative irradiation and feel that the best results at present can be obtained by the complete operation or by the complete operation and postoperative irradiation.

My associates and I have had a very limited experience in this clinic with excision of the breast only and have taken the point of view that it is an illogical operation in most instances because it is too much of an operation for a benign lesion and not enough of an operation for cancer. In this series there are nine patients who were subjected to excision of the breast only or excision of the breast and pectoral muscles but not the axillary dissection. Of these nine, four are well, four died of cancer and one died of another cause. The average length of time after operation in the four patients who are well is two years and eleven months (table 15). Of these nine patients, four received preoperative irradiation, and three are well (tables 16 and 17). The

TABLE 16.—*Results in Patients Subjected to Preoperative Irradiation Followed by Excision of the Breast*

Total number of patients.....	4
Well, no recurrence.....	3 (75%)
Average duration of time since irradiation.....	3 yr., 5 mo.
Death from cancer.....	1
Duration of life after irradiation.....	5 mo.
Duration of life after operation.....	2 mo.

average length of time since irradiation was begun is three years and five months. There were five patients in the group of nine who received no preoperative irradiation (tables 17 and 18). One patient is well two years and seven months after operation, three died of cancer (average duration of life since irradiation, three years) and one died of another cause in two years and eleven months without any clinical evidence of recurrence of metastases.

From these figures alone, which of course are limited, there is no actual proof that preoperative irradiation followed by simple excision of the breast is not as good as preoperative irradiation followed by the complete operation, yet if the reader will refer again to table 8 he will find that 44 per cent of the patients who had preoperative irradiation followed by the complete operation had demonstrable metastases in the axillary glands, and personally I feel very strongly that there should be no restriction of the complete operation because of preoperative irradiation.

The surgeon will have one opportunity only to cure a patient with carcinoma of the breast. When a clinically benign tumor proves in a frozen section to be cancer or is suggestive of cancer, he has the choice of doing the complete operation at once or closing the wound, giving

preoperative irradiation and after the proper interval of time doing the complete operation. In the doubtful cases, while the irradiation is going on the section can be submitted to other pathologists for their opinions. When the sections show cancer, even though all palpable evidence of disease was completely removed for biopsy, for the present anyway, I still feel that the complete operation should follow.

TABLE 17.—*Data on Patients Subjected to Excision of Breast Only in Regard to Grade of Tumor and Tissue Culture*

Total number of patients.....	9
Number of patients subjected to preoperative irradiation.....	4
Well (tumors, grade 1, 2, 2).....	3
Death from cancer (grade 3).....	1
No preoperative irradiation.....	5
Well (tumor, grade 3).....	1
Death from cancer (grade 2, 3 and no tissue from 1).....	3
Lost from observation (no tissue).....	1
Tissue culture	2
Negative (preoperative irradiation).....	1
Inaccurate (preoperative irradiation).....	1

TABLE 18.—*End-Results in Patients Subjected to Excision of Breast Without Preoperative Irradiation*

Total number of patients.....	5
Well, no recurrence.....	1 (20%)
Duration of time since operation.....	2 yr., 7 mo.
Death from cancer.....	3 (60%)
Average duration of life after operation.....	3 yr.
Death from other cause.....	1
Duration of life after operation.....	2 yr., 11 mo.

TABLE 19.—*End-Results for Patients in Group 5*

Total number of patients.....	41
Well	4 (9%)
Average duration of time since admission to clinic.....	1 yr.
Death from cancer.....	26 (63%)
Average duration of life after admission to clinic.....	1 yr., 4 mo.
Death from another cause (suicide).....	1 (2%)

The chances of curing a recurrent carcinoma of the breast are so small that I have about decided no longer to advise operation. Of the forty-one patients with recurrent carcinoma in this series, only four (9 per cent) are well, and the average length of time since these four were admitted to the clinic is only one year (table 19). Some of these recurrent carcinomas will be operable and present an apparently favorable prognosis, but the fact alone that they are recurrent almost excludes any possibility of a cure by surgical measures or by preoperative irradiation and surgical treatment. Perhaps even in this group it may be wise to treat by irradiation only.

GASTRIC SURGERY AND GASTROSCOPY

DIFFERENTIAL DIAGNOSIS OF BENIGN AND MALIGNANT LESIONS;
OPERABILITY OF TUMORS AS DETERMINED BY GASTROSCOPY;
EARLY DIAGNOSIS OF GASTRIC CARCINOMA;
THE POSTOPERATIVE STOMACH

RUDOLF SCHINDLER, M.D.

Visiting Professor of Medicine at the University of Chicago

AND

NORMAN GIERE, M.D.

Assistant Resident of the University of Chicago Clinics
CHICAGO

The purpose of this paper is to show the usefulness and value of gastroscopy to the surgeon.¹ The following questions will be discussed: 1. Is a lesion of the stomach, which has been diagnosed by other methods, a benign ulcer or a carcinoma? 2. Is cancer of the stomach operable or not? 3. Of what value is gastroscopy in the early diagnosis of carcinoma, and may it improve the operative results? 4. What are the reasons for the abdominal distress which so frequently follows operations for gastric lesions?

We shall not include the results of the numerous gastroscopies carried out by one of us (R. S.) in Germany, because the records cannot be controlled. Thus we shall restrict ourselves to the gastroscopic examinations carried out at the Billings Hospital of the University of Chicago Clinics.² The majority of the patients were referred for gastroscopy by Dr. W. L. Palmer, chief of the gastro-intestinal department. A total of four hundred and sixty-five gastroscopies were performed; forty-one of the patients on whom gastroscopy was per-

All surgical work was done by the Surgical Department of the University of Chicago Clinics unless otherwise stipulated. Splendid cooperation was given by the Department of Radiology (Dr. Hodges).

1. Schindler, R.: *Lehrbuch und Atlas der Gastroskopie*, Munich, J. F. Lehmanns, 1923; *Diagnostic Gastroscopy*, with Special Reference to the Flexible Gastroscope, J. A. M. A. **105**:352-355 (Aug. 3) 1935; A New Tube for Anaesthetization of the Hypopharynx, *Am. J. Digest. Dis. & Nutrition* **2**:281-282 (July) 1935; *Gastroscopy in Thirty Cases of Gastric Neoplasm*, *Arch. Int. Med.* **32**:635-646 (Oct.) 1923. Moutier, F.: *Traité de gastroscopie et de pathologie endoscopique de l'estomac*, Paris, Masson & Cie, 1935.

2. The flexible Schindler-Wolf gastroscope was used in all examinations. This instrument may be obtained from the Zeiss Corporation, 485 Fifth Avenue, New York.

formed also received surgical treatment, and it is this group which furnishes the material for our paper. Biopsic control was possible in twenty cases; the remaining twenty-one are presented because of the interesting observations which they offer. Since more than one gastroscopy was done on many of our patients, a total of seventy-eight gastroscopies were performed on our group of forty-one patients. We realize that complete presentations of such a large amount of material tends to make the paper rather detailed, but since so little work has been done relative to the value of gastroscopy in cases involving operations for gastric lesions, we believe that surgeons will appreciate these details as being valuable for purposes of study.

A. GASTRIC ULCER AND CARCINOMA VISUALIZED BY GASTROSCOPY BEFORE OPERATION

DIFFERENTIAL DIAGNOSIS

Benign Ulcer.—The difference between a benign and a malignant pyloric obstruction is characteristic gastroscopically, although it is well known that a duodenal ulcer cannot be seen with the gastroscope. Recent statistics indicate that a prepyloric ulcer is very rare and is generally carcinomatous. We have never seen one gastroscopically, but since the lesser curvature of the antrum is infrequently seen with the gastroscope, this observation is of less importance than is the experience of the pathologist and the surgeon. It is, however, sometimes difficult even for the pathologist to decide, in the gross specimen, whether a pyloric obstruction is benign or malignant. In all instances of carcinomatous obstruction of the pylorus the protruding carcinomatous tissue was seen by gastroscopy, whereas in cases of ulcer of the pyloric channel or of benign pyloric obstruction the pylorus was usually not seen because adhesions draw it backward so as to remove it from the field of vision. It may be mentioned that in cases of uncomplicated duodenal ulcer the pylorus is often seen very well, and its activity shows no deviation from the normal. The following case illustrates the uncertainty of diagnosis in many of these cases as well as the difficulty of deciding definitely the nature of the lesion by examination of the gross specimen.

CASE 1.—History.—A white Canadian man aged 38, seen on Aug. 14, 1934, had suffered from epigastric distress for one year without remission. He had lost 35 pounds (15.9 Kg.) in weight and had a sensation of tenderness and fulness which became so acute at times that he felt he would burst. When he induced vomiting, he obtained relief. The vomitus practically always contained undigested food. At no time were tarry stools noted, and there were no other complaints.

Physical Examination.—There was some tenderness in the epigastrium. A large peristaltic wave was seen which moved across the entire upper two thirds of the abdomen. No definite mass was felt. The other organs were normal.

Laboratory Examination.—One thousand, two hundred cubic centimeters of gastric fluid obtained after an Ewald test meal showed: free acid, 37; total acid, 59; lactic acid, 0, and blood, a trace. Microscopic examination of the contents gave normal results. The reaction of the stools to the benzidine test for blood varied from negative to 3 plus.

Roentgen Examination.—The roentgenogram was very suggestive of carcinoma of the antrum of the stomach, with obstruction, retention and dilatation. The condition was thought to be carcinoma of the antrum, but the possibility of an ulcer could not be ruled out.

Gastroscopy.—The stomach contained considerable fluid, which covered the greater curvature. The antrum was well seen, however, particularly in its greater curvature. The pylorus was not completely visible. The mucous membrane was somewhat moist and swollen, but there was no tumor visible; the musculus sphincter antri was very prominent. The mucosa of the body showed no pathologic changes. The gastroscopic diagnosis was gastritis of the antrum.

Clinical Impression.—On the basis of the clinical picture the condition was thought to be carcinoma of the stomach with pyloric obstruction.

Operation (August 20).—The stomach was found to be greatly enlarged, and a hard inflammatory mass was felt at the pylorus. The pyloric antrum and the first part of the duodenum were resected. The duodenum and the end of the stomach were closed, and a posterior gastro-enterostomy was performed with the first part of the jejunum.

Pathologic Examination.—The base of the ulcer was necrotic and yellow and extended well into the wall of the stomach. There were radiating fibrous strands and adhesions about its outer aspect in which there were palpable lymph nodes indicating carcinomatous invasion. Section of the wall showed it to be thickened and to contain translucent and fibrous material. Microscopic examination of the ulcer showed it to be benign.

The diagnostic course of this case is typical. A definite obstruction of the pylorus gave the clinical impression that a carcinoma was present; roentgen examination also indicated carcinoma, although the roentgenologist stated that a benign ulcer could not definitely be ruled out. The surgeon, however, thought that the lesion which he removed was benign, but on gross examination it was thought to be carcinomatous. Microscopic examination proved that the lesion was a benign ulcer. Since no tumorous tissue was seen at the pylorus on gastroscopic examination, we were safe in concluding that carcinoma was not present but that the obstruction was due to a benign lesion with secondary inflammation of the mucosa of the antrum.

After the operation gastroscopy was done three different times. The results will be discussed in section B.

The following case presents a general agreement concerning the nature of the lesion.

CASE 2.—History.—A man aged 47, seen on Oct. 9, 1934, stated that he had had complaints referable to the stomach for the past seventeen years with rather frequent vomiting but no pain. The past few years he had suffered from disten-

tion, which had been relieved by sodium bicarbonate. The appetite had remained good, although the patient had lost 25 pounds (11 Kg.) in the past year and a half.

Physical Examination.—Nothing abnormal was found.

Laboratory Examination.—Two hundred and thirty cubic centimeters of gastric fluid obtained after an Ewald test meal showed: free acid, 40; total acid, 94, and blood, 0. The stools gave a 4 plus reaction to the benzidine test for blood.

Roentgen Examination.—The roentgenogram showed a stenosing ulcer of the pyloric channel with a surrounding inflammatory reaction and resulting gastric retention. Early pyloric neoplasm could not be absolutely ruled out.

Gastroscopy.—The entire stomach, including the pylorus, was well seen. There were no pathologic changes present.

Clinical Impression.—On the basis of the clinical picture the condition was thought to be a duodenal ulcer with high grade stenosis.

Operation (December 8).—Operation was delayed because of the indecision of the patient. A large duodenal ulcer was found which produced almost complete pyloric stenosis. The lesion was situated on the posterior wall about 3 cm. distal to the pylorus. A posterior gastro-enterostomy was performed. No pathologic examination was possible. The patient returned to the clinic on Feb. 4, 1935; he had gained 5 Kg. and looked extremely well.

Although this case was evidently one of obstructive duodenal ulcer, a neoplasm could not be ruled out with certainty by roentgen examination, whereas the gastroscopic examination was conclusive, since the pylorus was well seen and no carcinomatous changes were visualized.

There was complete agreement in diagnosis of the following case.

CASE 3.—History.—A man aged 67 had suffered from pain in the epigastrium below the xiphoid process for the past twenty-five years, with restlessness, irritability and fatigue becoming prominent during the past two years. There was a loss of weight of 10 pounds (4.5 Kg.) during the past six months.

Physical Examination.—A mass was felt in the epigastrium above the umbilicus that moved with peristaltic waves, which were both visible and palpable.

Roentgen Examination.—The roentgenogram showed high grade pyloric obstruction, thought almost certainly to be the result of a chronic duodenal ulcer.

Gastroscopy.—It was difficult to find the pylorus, but finally the entire antrum and the lower half of the pylorus were well seen. The lower parts of the greater curvature were edematous, as were other parts of the stomach to a lesser degree. In the upper parts of the body red spots were seen. The diagnosis on the basis of the gastroscopic findings was superficial edematous gastritis.

Operation.—The wall of the stomach was found to be markedly thickened. There was definite scarring of the duodenum just beyond the pylorus. A posterior gastro-enterostomy was done, and the patient made an uneventful recovery.

The gastroscopic findings were typical of benign obstruction, especially the high grade edema of the antrum, which is seen only in this condition.

In the differential diagnosis of gastric ulcer other signs are important. It is frequently impossible to differentiate such an ulcer from a carcinoma even in the gross specimen, and one may think that it is just as

EXPLANATION OF PLATE

A, gastroscopic picture of the penetrating benign ulcer of the lesser curvature of the stomach in case 4. The edge of the crater-like ulcer is sharp, and the cardiac part of its floor is brownish. Blood is shown oozing from the lowest part of the floor and accumulating in the dependent part (upward in the picture). The adjacent mucosa is excessively swollen and inflamed. Compare this illustration with figures 1, 2, 3 and 4.

B, gastroscopic picture of the infiltrating carcinoma with ulceration in the case in which operation was not performed. In the center of the picture there is a dark red ulceration. All the other parts of the stomach visualized with the gastroscope were stiff and infiltrated, and the surface was necrotic. The necrosis extended up to the cardia. Compare this illustration with figure 8. Gastroscopy proved immediately the inoperability of the tumor.

C, gastroscopic picture in case 7, showing ulcerative carcinoma. The ulcer is filled with brown clotted blood. The gray ridge discloses the malignant character of the ulcer.

D, gastroscopic picture, also from case 7, made four weeks after *C*. The ulcer as well as the niche (fig. 5) were shallower, but at the pyloric side a nodular infiltration was seen. Compare this picture with figures 6 and 7.

E, gastroscopic picture in case 13, showing an ulcerated carcinoma around the pylorus with a sharply limited wall. The fold above the tumor is the "angulus." The whitish areas are remainders of food. Radical operation was possible. Compare this picture with figures 9 and 10.

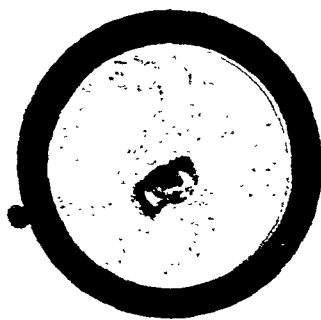
F, gastroscopic picture in case 14, showing the patent gastro-enterostomy opening in the center. Intestinal juice flows into the stomach. At the side of the stoma there is a white ulcer larger than the stoma. A silk suture is seen coming out of the mucosa and hanging freely into the cavity of the stomach.

G, gastroscopic picture in case 21, showing the opening phase of the gastro-enterostomy stoma. The objective of the gastroscope is turned toward the anterior wall; the pylorus, which is well seen in figure 12, is not visible. The circular Kerkring folds of the jejunum are seen.

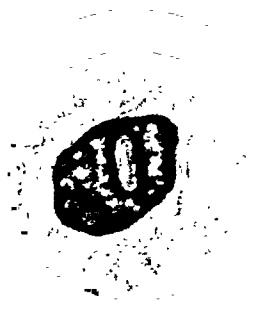
H, gastroscopic picture in case 26, showing a considerable portion of the jejunum in the right lower quadrant. About 2 cm. below the margin a crater-like deep ulcer is seen. The margin is partly covered with pus, and about it mucosal hemorrhages are seen.



A



B



C



D



E



F



G



H

PLATE

difficult by gastroscopic examination. This is definitely not so. As a rule these ulcers are seen distinctly gastroscopically, and the circulating blood makes the coloring quite characteristic. It can be further observed that the edge of a carcinoma is never as sharp as it appears to be in the gross specimen after resection and also that the floor of a carcinomatous ulcer blends gradually with the surrounding mucous membrane. If the edge is entirely sharp the lesion may be diagnosed as a benign ulcer; if the edge is not so sharp and the floor is ragged, dirty and irregular, it may safely be called a malignant ulcer. The sharpness of the wall is a more important differential point than is the abnormality of the floor of the lesion.

CASE 4.—History.—A man aged 51, seen on Oct 24, 1934, about five years previously had an attack of epigastric distress which was thought to be the result of a peptic ulcer. He was placed on the Sippy diet, and the pains disappeared. About one month before he vomited and felt very weak. He placed himself on a milk diet, during which time his distress continued, and his emesis occurred at least twice daily. He had lost 24 pounds (10.9 Kg.) in weight during the past two months.

Physical Examination.—Moderate tenderness was felt in the epigastrium. All other findings were normal.

Laboratory Examination.—One hundred and sixty-five cubic centimeters of gastric fluid obtained after an Ewald test meal showed: free acid, 35, and total acid, 51. Microscopic examination of the contents gave normal results. The stools gave a 4 plus reaction to the benzidine test for blood.

Roentgen Examination (October 26).—There was an enormous penetrating ulcer at the lesser curvature of the stomach; the film showed the thickened gastric rugae of the opposite wall. The size of the lesion and the mucosal changes indicated, but did not prove, the possibility that the ulcer might be carcinomatous (fig. 1).

First Gastroscopy (October 30).—On the lesser curvature of the stomach a large ulcer was seen just above the angulus. It was very deep, and its edges were sharp and undermined. The color of that part of the floor which lay toward the cardia was reddish brown, whereas that near the pylorus was whitish gray. In this region of the ulcer fresh light red blood was oozing from the base and flowed toward the cardiac side of the floor; the mucous membrane of the stomach in this region was definitely spotted. Slightly nearer the cardia the mucous membrane of the anterior wall appeared swollen; it did not reflect light and appeared to be divided into sections by small creases. The entire lower parts of the anterior wall also presented these changes and further disclosed one rather large hemorrhage. On the other hand, all portions of the greater curvature of the posterior wall and of the upper parts of the anterior wall were normal. On the basis of the gastroscopic findings a diagnosis was made of (1) deep bleeding benign ulcer of the lesser curvature of the body above the angulus and (2) marked hypertrophic hemorrhagic gastritis of the anterior wall. (See A in the color plate.)

Second Gastroscopy (November 19).—The ulcer was instantly seen. It had lost much of its depth but was still large. Its edge was quite sharp, and the floor was dirty gray. Whitish membranes passed from the mucous membrane of

the cardiac side of the ulcer to its floor. The antrum and pylorus were normal. The hypertrophic gastritis of the anterior wall was as distinctly seen as at the last examination and showed no improvement. The other parts of the stomach were normal (fig. 2).



Fig. 1 (case 4).—Roentgenographic picture of the stomach. Because of the size of the niche, the diagnosis of a malignant growth could not be ruled out. Compare this picture with the gastrosopic picture in *A* of the color plate. Gastrosopically, the benign nature of the lesion was evident.

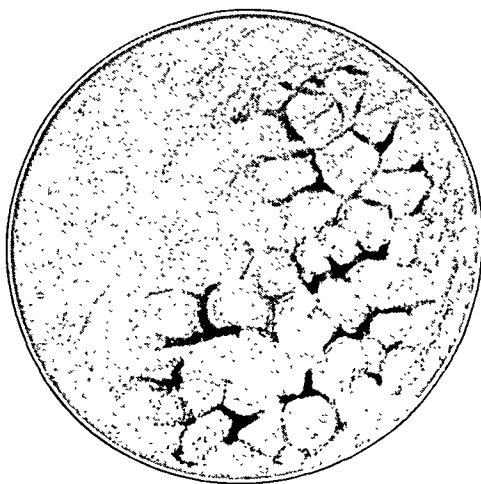


Fig. 2 (case 4).—Severe hypertrophic gastritis in the vicinity of the ulcer, as visualized gastrosopically. The mucous membrane is swollen and nodular ("cobblestone formation"), and hemorrhage is seen (see left side of illustration). (From Schindler, R.: *Am. J. Digest. Dis. & Nutrition* 2:655 [Jan.] 1936.)

Second Roentgen Examination (November 26).—There was no diminution in the size of the large penetrating ulcer of the lesser curvature of the stomach.

Clinical Impression.—Considering the history of symptoms of long standing, the ulcer was believed to be benign. The patient was advised to have an operation.

Operation (November 30).—A large ulcer was found situated high on the lesser curvature. Its crater was large enough to admit the tip of a thumb. Gastric resection was done, with uneventful recovery.

Pathologic Examination.—About 5 cm. above the pylorus there was a deep penetrating ulcer, measuring 2.75 by 2 cm., with a sharply defined border and a punched-out appearance. The edges were slightly undermined. The base consisted of adhesive omental tissue. The rugae which radiated from the ulcer were much flattened for an area 8 cm. in diameter around the lesion. This region appeared hyperemic, swollen and hypertrophic (fig. 3). The border of the ulcer was raised and indurated but was not stony hard. The rest of the mucosa appeared practically normal except for petechiae. Section through the edge of the crater of the ulcer showed an ulcer penetrating through all walls of the stomach; the floor was flat and composed of fibrosed omentum, whereas the sides



Fig. 3 (case 4).—Resected gastric ulcer. Compare this illustration with figure 1 and with *A* in the colored plate. The gastritic nodules seen gastroscopically can be observed in the gross specimen.

were steep and abrupt. Round cell and eosinophilic infiltration was seen involving the fibrosed omentum and the wall of the stomach. Sections from various other parts of the stomach showed varying degrees of eosinophilia and polymorphonuclear invasion but no evidence of ulceration or malignancy (fig. 4).

In this case the clinical picture and the gastroscopic picture were in complete agreement. It should be noted, however, that the roentgenologist considered the possibility of a malignant ulcer more likely, whereas the gastroscopic picture definitely showed the ulcer to be benign. Another point of interest is that the ulcer appeared shallower on the second gastroscopic examination, whereas there was no difference in the results of the two roentgen examinations. It cannot be proved, of

course, which impression was correct. The microscopic specimen confirmed the gastroscopic findings of severe hypertrophic gastritis around the ulcer.

Because of the fact that so many of the deep ulcers which were observed gastroscopically healed under the medical management of



Fig. 4 (case 4).—Photomicrograph of a section made through the gastritic area shown in figure 2. Note the proliferation of the surface epithelium and the tremendous interstitial infiltration without alteration of the long gastric glands.

Dr. Palmer and his staff, we are unable to report on a greater number of cases in which operation was performed. In some cases we could follow this healing process through numerous gastroscopies, until complete epithelization took place.

Carcinomas.—CASE 5.—*History.*—The patient, aged 70, from the Cook County Hospital, was referred for gastroscopy by Dr. Harry Singer because of weakness and tarry stools.

Roentgen Examination.—The roentgenogram showed a small pancake-like infiltrative lesion of the prepyloric area with nichelike formation of the lesser curvature. It was uncertain whether the lesion was an ulcer or a carcinoma.

Gastroscopy (April 17, 1935).—Just beneath the angulus a small, jagged prominence was seen during inspiration, the color of which was darker than that of the angulus itself. The mucous membrane of the lesser curvature above the angulus was without marked changes, although we had the impression that it was stiff and infiltrated. In spite of the fact that the involved area was seen only for parts of a second, we were of the opinion that the condition must be a carcinoma of the lesser curvature of the antrum. The size of the tumor could not be estimated.

Operation (June 30).—Resection was done for carcinoma. Microscopic examination of the specimen showed ulcerative adenocarcinoma.

This case illustrates the difficulties of making a diagnosis even with gastroscopy. The lesion was situated in that part of the stomach which is the most difficult to see, i. e., the "blind" area of the lesser curvature of the antrum. A benign ulcer would never have been seen, although in some cases radial folds converging toward the angulus, causing the appearance of a sharp angle instead of the usual parabolic line, may indicate a hidden ulcer. In this case we were fortunate to see part of the lesion, even if for only a part of a second. This indicated with certainty that the lesion was malignant. Nevertheless, it must be admitted that a small carcinoma of this region may be overlooked, although we have never seen such a case.

CASE 6.—*History.*—A woman aged 38, seen on Oct. 12, 1934, complained of vomiting for the past two years from once to three times weekly. About three months before the present examination the vomiting increased in frequency, and two weeks before it occurred after almost every meal. The vomitus contained some undigested food and "brown foamy stuff" which tasted bitter. Recently this had been followed by burning pains around the umbilicus. The patient's appetite had been good, but for the past two weeks she had been afraid to take food because of the pain and vomiting which followed. There had been a loss of weight of 22 pounds (10 Kg.) in the last two months, unassociated with loss of strength. The patient was nervous and restless.

Physical Examination.—No abnormalities were found.

Laboratory Examination.—The red cell count was 5,040,000 and the white cell count 7,100. Gastric fluid obtained after an Ewald test meal showed: free acid, 9, and total acid, 106 (questionable). The stools gave a 4 plus reaction to the benzidine test for blood.

Roentgen Examination.—The roentgenogram showed a large penetrating crater on the lesser curvature of the stomach. The mucosal folds about this lesion and on the greater curvature were thickened and stiffened. The patient complained of marked tenderness over this area, and at times it seemed that an indefinite mass could be palpated. We were unable to differentiate definitely between ulcer

with associated regional gastritis or ulcer with associated carcinomatous infiltration. The impression was that there was a penetrating ulcer with associated regional gastritis. Carcinomatous infiltration could not be absolutely ruled out. The suggestion was made that the patient be referred for gastroscopy.

Gastroscopy.—A few centimeters above the angulus a large prominence of the lesser curvature was seen. An ulcer of irregular shape, with very irregular edges and surrounded by a definite wall, was found. There was no distinct edge, the ulcerated surface passing gradually into the mucous membrane of the wall, which was swollen and contained pigment spots.

On the basis of the examination it was decided that this was not the picture of a benign ulcer; a malignant lesion of the lesser curvature was suspected.

Operation (October 16).—A large carcinomatous mass was found involving the lesser curvature of the stomach extending almost to the cardia. Practically the entire stomach as well as a large section of the transverse mesocolon was resected. A posterior gastro-enterostomy was done between the first part of the jejunum and the small stump of the remaining portion of the stomach. Recovery was uneventful.

Pathologic Examination.—A crateriform ulcer, 4 by 3.5 by 1.5 cm., was seen. The base of the ulcer extended through much of the wall of the stomach and probably into the adherent omentum. Microscopic examination of a section through the margin of the large ulcerating lesion showed normal mucosa at the fundus which abruptly became necrotic, giving the typical appearance of the crater of an ulcer. Beneath the crater the wall of the stomach was composed of dense edematous fibrous tissue. The entire wall was infiltrated by carcinoma cells, varying greatly in size and appearance and showing areas of "colloidal" transformation with numerous signet ring cells. A section through the wall farthest from the lesion showed no carcinoma but a diffuse infiltration of the muscularis by polymorphonuclears.

In this case, in which the symptoms were of long duration, the roentgen examination could not establish a differential diagnosis between a benign and a malignant lesion. A benign lesion seemed to be more probable; however, the roentgenologist suggested the gastroscopic examination, which definitely proved the malignancy of the lesion. This close cooperation between the roentgenologist and the gastroscopist seems to us to show the proper attitude and the one which is to the best interests of the patient. Each method complements the other; they should most certainly not be regarded as methods of competition. Although in this case the development of a carcinoma from a benign ulcer cannot be proved, it is possible. It is quite certain that an earlier gastroscopic examination would have revealed the beginning carcinomatous formation. This case will again be mentioned in the section concerning operability of carcinomas and the value of early diagnosis in gastric carcinoma.

We consider the following the most important case presented in this paper.

CASE 7.—History.—A man aged 71, seen on June 4, 1935, three years before suffered from gnawing epigastric distress one or two hours after eating. A post-

genogram demonstrated an ulcer, but the patient was not informed whether it was duodenal or gastric. He was placed on a diet, whereupon the distress disappeared. He had no further difficulties until about four months before the present examination, at which time he had daily distress which was relieved by the ingestion of powders or food. There was no loss of weight.

Physical Examination.—Bronchiectasis and obliterative pleuritis of the left side of the chest were found to be present. A roentgenogram of the heart showed the organ to be 29 per cent oversized. No mass could be palpated in the abdomen, and there was no tenderness.

Laboratory Examination.—The histamine test showed free acid (28) after thirty minutes. The stools gave a negative to a 4 plus reaction to the benzidine test for blood.

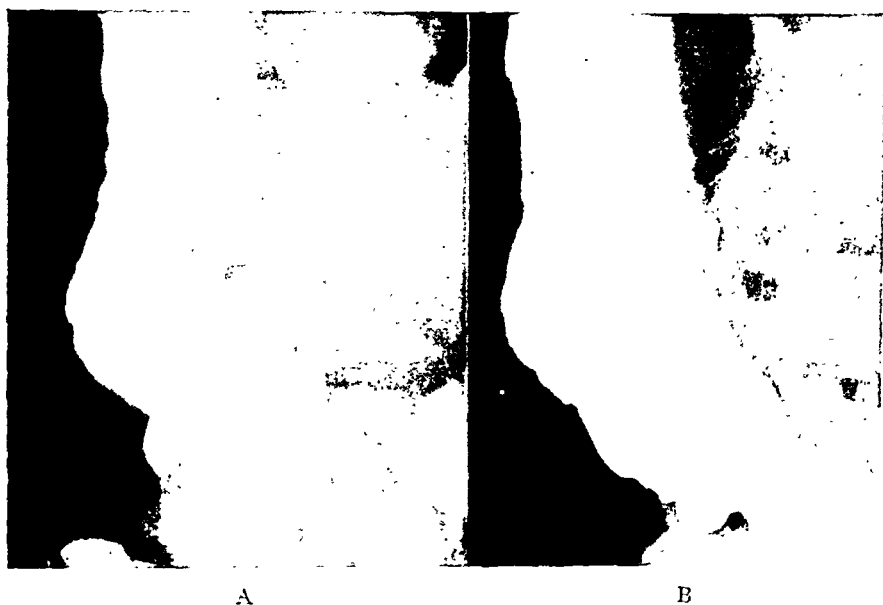


Fig. 5 (case 7).—*A*, roentgenogram made on June 21, 1935. The large niche of the lesser curvature was believed to represent a benign ulcer. *B*, roentgenogram made nineteen days later. The markedly reduced size of the niche seemed to prove definitely the benign nature of the lesion. Compare with *C* and *D* in the color plate, *C* corresponding with figure 5 *A* and *D*, with figure 5 *B*.

Roentgen Examination.—We shall give the results of all examinations in connection with this case. It may be mentioned here that the fifth and sixth readings were proved to be incorrect. They were revised after comparison with the gross specimen.

June 17: A large penetrating ulcer of the cardiac end of the lesser curvature of the stomach was seen.

June 21: A benign penetrating ulcer of the cardiac end of the lesser curvature of the stomach was observed (fig. 5 *A*).

July 9: The crater was smaller (fig. 5 *B*).

July 19: The crater was becoming smaller

August 9: The ulcer of the cardiac end was again becoming larger. A second lesion was present at the lower end of the lesser curvature of the stomach. One or both of the lesions were thought to be neoplastic.

August 26: The penetrating ulcer was still present. The second lesion was present at the lower end of the lesser curvature. The latter was probably carcinomatous.

October 31: There was no second lesion. The large crater was still present at the cardia of the lesser curvature.

First Gastroscoy (June 22).—A sharp picture of the lesser curvature was obtained. There was a large crater-like ulcer, the edge of which was rather sharp, but the whole cavity was filled with blood coagula. In this blood was seen a grayish ridgelike prominence. The mucous membrane surrounding the ulcer was partly thinned and partly swollen. On the basis of the gastroscopic findings a diagnosis of ulcer-like carcinoma of the lesser curvature of the stomach was made. In spite of the high location, the carcinoma seemed to be so well limited that a radical operation was not completely out of the question. (See C in the color plate.)

Second Gastroscoy (July 8).—The pyloric region was instantly seen. About the entrance of the antrum the mucous membrane pattern was extremely irregular. On the anterior wall of the greater curvature there were nodes of varying size. On the lesser curvature, just above this point, an elevation was observed, on top of which was an ulcer. The edge of this ulcer lying toward the pylorus was not sharply defined, but all other edges were well demarcated. The floor was grayish white and was not bleeding. The slope of the elevation was extremely reddened and appeared to be edematous. The nodular changes at the entrance of the antrum were too large to permit a diagnosis of nodular gastritis. Carcinomatous infiltration was suspected. Furthermore, the ulcer of the lesser curvature did not have the appearance of the usual benign ulcer because of its situation on an elevated area and because one part of its edge was not sharply defined. For these reasons we believed that a carcinomatous lesion was present which was well limited toward the cardiac portion of the stomach but appeared to be progressive toward the pyloric part. Radical operation seemed to be possible at this stage. (See D in the color plate.)

Operation (November 4).—An ulcerating lesion was felt in the lesser curvature upward toward the cardia. About seven eighths of the stomach was resected. The patient died on November 8 from bronchopneumonia. Permission for autopsy was not given.

Pathologic Examination.—Carcinoma was found on the lesser curvature. Microscopic examination showed colloidal carcinoma of the mucosa, well defined against the muscularis mucosae but invading the lymph vessels of the submucosa. The distant parts of the wall of the stomach showed dilatation of blood vessels and edema of the submucosa, which was three times thicker than usual (figs. 6 and 7).

This case demonstrates the superiority of gastroscopy over all other methods in arriving at this diagnosis. The history, and particularly the roentgenogram, suggested a benign lesion. Even after knowing of the presence of carcinoma, as proved microscopically, no one could find the least evidence of it either in or hidden by the mucosal folds, which the roentgenogram showed to be radiating from the ulcer. The pathologic examination offers the explanation: The carcinoma was almost noninvas-

ing. It did not even invade the muscularis mucosae. The gastroscopic picture, however, was definite, even after the first examination, at which the crater of the ulcer was seen filled with blood. It must be pointed out



Fig. 6 (case 7).—Gross specimen of a carcinoma of the lesser curvature of the stomach after resection. Compare with *C* and *D* in the color plate. The resection was made four months after the second gastroscopy.



Fig. 7 (case 7).—Photomicrograph of a section made through the carcinoma shown in figure 6. Compare with *C* and *D* in the color plate. A colloid carcinoma of the mucosa is well defined against the muscularis mucosa but is invading the lymph vessels of the submucosa.

that much experience is necessary for such endoscopic accuracy; this is naturally also true of other diagnostic procedures. Here again it is possible, but it cannot be proved, that the carcinoma developed from a

preceding ulcer. The gastroscopic findings were so exact that even the enlargement of the mucosal blood vessels were seen (redness of the wall), and the edema of the gastric wall was described. The patient was not anxious to have an operation, and because he was a poor operative risk he was not urged too strongly. The fact that the niche in the roentgenogram became shallower during the observation while the carcinoma was progressive seemed to us to be important. Such cases have been described by Bloomfield.³ It is obviously dangerous to assume that a niche is produced by a benign ulcer because it becomes shallower during roentgen observation of a few weeks; early gastroscopy is indispensable. We shall later discuss the fact that here a true "early" diagnosis of a gastric carcinoma was made by means of gastroscopy.

Conclusions.—Operation was performed on seven patients, in each of whom it was not quite certain clinically whether a benign or a malignant ulceration of the stomach was present. In four of these cases the ulcer was proved microscopically to be benign; in all of these cases the roentgen examination gave doubtful results, and in two carcinoma was thought to have been present. Gastroscopy established a correct diagnosis in every instance.

In three of the original cases the lesion was proved to be carcinomatous. The roentgen diagnosis was incorrect in one instance and uncertain in the remaining two. The gastroscopic diagnosis again was correct in each case. The case in which a malignant ulcer was diagnosed gastroscopically but in which the ulcer was thought to be benign, both by clinical impression and by the fact that the lesion became shallower on repeated roentgen examinations, will be discussed later. The splendid cooperation between the roentgenologist and the gastroscopist was appreciated as being of great value.

OPERABILITY OF CARCINOMA AS DETERMINED BY GASTROSCOPY

Inoperable Tumors.—The inoperability of a tumor is dependent not only on the local gastric findings but also on the general condition of the patient and on the presence or absence of metastases. Nevertheless, the inoperability may become evident instantly by gastroscopy. It may be shown that the tumor is not sharply defined and that the infiltration extends too high to allow even a radical operation. This can usually be demonstrated better by gastroscopy than by roentgen examination. We believe that no surgeon considers the exploratory operation satisfactory in cases in which the condition proves to be inoperable. Bier has said that exploratory laparotomy in cases of gastric cancer is murderous. We believe, however, that before the introduction of gastroscopy

3. Bloomfield, A. L.: Diagnosis of Early Cancerous Changes in Peptic Ulcer. J. A. M. A. **104**:1197-1201 (April 6) 1935.

exploration was warranted in many cases but that now it should seldom be necessary after careful examination by a well trained gastroscopist.

CASE 8.—History.—A man aged 64, seen on March 6, 1935, suffered from epigastric pain for ten weeks.

Physical Examination.—A hard movable mass was found in the left upper quadrant of the abdomen.

Laboratory Examination.—The gastric contents showed: free acid, 0. and total acid, 15.

Röntgen Examination (March 11).—A large gastric carcinoma, probably of the medullary type and probably located on the posterior wall, was thought to be present. The lesion extended high along the greater curvature, possibly so high as to be inoperable.

Gastroscopy (March 8).—The nodular angulus was overhanging the entrance of the antrum so that only a small portion of the antrum could be seen. The angulus and the lesser curvature above the angulus were stiff and infiltrated and showed numerous nodules. Color changes were present. The same findings were seen in the posterior wall, and, to a less extent, in the lesser curvature. There was no sharp limit of the mucous membrane, but we had the impression that from about 8 cm. beyond the cardia the mucous membrane was rather normal. On the basis of the gastroscopic findings a diagnosis of infiltrating cancer without sharp limits was made. In spite of the fact that the cancer was situated rather low in the stomach, its limits were not sharp, and because of this we believed that the chances of a successful operation were poor.

Operation.—A huge carcinoma was found involving the distal two thirds of the stomach. There were metastases along both the greater and the lesser curvature. The condition was considered inoperable. The patient died on March 18 of pulmonary embolism.

Autopsy.—Ulcerating carcinoma of the prepyloric area of the stomach was found arising in the posterior wall and permeating the wall of the stomach; it extended radially to the perigastric, pancreatic and periaortic lymph nodes from the level of the cardia to that of the renal vein, etc. Microscopic examination showed that the carcinoma had arisen in the gastric mucosa; it had spread through the lymphatics and permeated the wall of the stomach. The neoplasm consisted of atypical hyperchromatic epithelial cells which were growing in masses but with a definite tendency to tubule formation in places. The lymphatic spaces in the serosa of the stomach were dilated and filled with masses of carcinoma cells.

The carcinoma was considered inoperable because of both roentgen and gastroscopic observations; the latter showed infiltration and lack of sharp limitation of the lesion. Later the microscopic examination showed the diffuse infiltration of the wall of the stomach and the invasion of the lymphatic spaces of the serosa. Operation was attempted; the patient died from embolism.

CASE 9.—History.—A man aged 63, seen on Jan. 7, 1935, suffered from abdominal distress for eight months, with belching and regurgitation. There had been loss of appetite and weakness of about one year's duration.

Physical Examination.—An epigastric mass, unmovable and about 4 cm. in diameter, was felt.

Roentgen Examination (January 8).—The picture was that of polypoid carcinoma involving the central portion of the stomach. The extreme cardiac end and the pylorus were believed to be free from infiltration.

Gastroscopy (January 9).—A hard mass was felt a few centimeters below the cardia on the passage of the Ewald tube. The gastroscope could be introduced just beyond the cardia. In the lesser curvature a hemorrhagic infiltration was seen. The diagnosis was a large neoplasm of the upper part of the stomach, infiltrating the lesser curvature.

Operation (November 2).—A large thickened mass involving most of the greater curvature and most of the posterior wall and extending from the lower third to within about 2 cm. of the cardiac orifice was found. It was decided that an attempt at subtotal gastrectomy could not be successful since the stomach was adherent to the carcinoma, which had grown beyond the confines of the stomach. High voltage roentgen therapy improved the condition.

There was general agreement concerning the nature of the lesion. The carcinoma extended almost up to the cardia. The inoperability was best shown by gastroscopy. Such infiltrating lesions without sharp demarcation in the upper part of the stomach must always be considered as being unfavorable for operation, especially if the gastroscope cannot be completely introduced. It is questionable whether gastroscopy was not contraindicated in this case. Our diagnosis of infiltration of the lesser curvature of the stomach was shown to be incorrect. This case, with others, has influenced our new conception of gastroscopic orientation in the upper parts of the stomach.

CASE 10.—History.—A patient aged 50, seen on April 24, 1935, suffered from weakness and a constant dull aching pain in the epigastrium for two months. He had lost 30 pounds (13.6 Kg.) in weight since Jan. 1, 1935.

Physical Examination.—No abnormalities were found.

Laboratory Examination.—The gastric fluid after the injection of histamine showed no free acid. The stools gave a 4 plus reaction to the benzidine test for blood. The blood showed 60 per cent hemoglobin and 4,000,000 red blood cells.

Roentgen Examination (April 26).—The roentgenogram showed a large carcinoma situated high on the lesser curvature of the stomach with a ragged crater at the center.

Gastroscopy (April 27).—At the cardia marked resistance was felt, but it was possible to bring the instrument into the stomach. Instantly a large tumor was seen on the anterior wall invading the lesser curvature. It extended from about the region of the angulus up to the cardia. The bleeding protrusion was not sharply limited and contained an irregular yellowish white ulceration. A diagnosis of a large carcinoma of the anterior wall and lesser curvature, not sharply limited, involving the cardia, was made. In our opinion the condition was inoperable but probably suitable for roentgen therapy.

Operation (April 30).—The stomach was examined and found to be involved by a carcinoma which extended along the lesser curvature, reaching up to the esophagus and infiltrating the gastrohepatic mesentery. Metastases were found in the liver. The involved portion of the stomach was fixed to the posterior parietes so that it could not be brought down and lifted out into the field. The patient was discharged on May 27 and died on July 3.

Roentgen examination and gastroscopy showed a carcinoma situated high up on the lesser curvature of the stomach. Gastroscopy gave evidence of its inoperability.

A 75 year old man had epigastric distress for one year, which was relieved by food. Physical examination gave essentially negative results except for a slight enlargement of the heart accompanied by an apical systolic murmur. The gastric fluid showed no free acid. The stools gave a 4 plus reaction to the benzidine test for blood. Roentgen examination revealed a penetrating ulcer of the lesser curvature of the stomach with infiltration of the lesser curvature (fig. 8). The roentgenologist felt that the extreme cardiac end of the stomach was not involved, but the examination was difficult because of the inability of the patient to relax. The gastroscopic findings follow: The pylorus and the antrum were about normal.

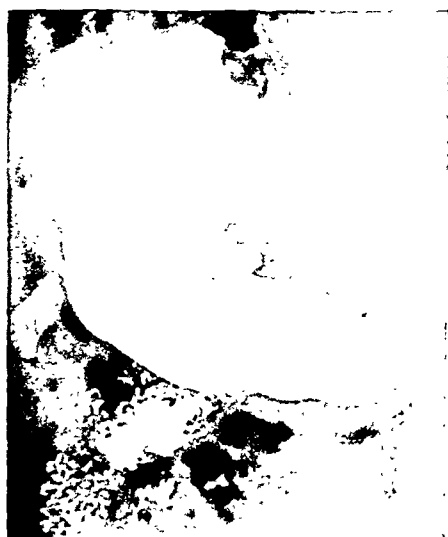


Fig. 8.—Roentgenogram in a case in which operation was not performed because gastroscopy (see *B* in the color plate) definitely proved the inoperability of the growth.

Just above the angulus a grayish white tumor appeared involving the lesser curvature, the anterior wall and the greater curvature. Protruding nodes were seen on the lesser curvature only. In other parts there were a whitish infiltration and rigidity of the entire mucous membrane. This picture was seen just below the cardia, although even the cardia was somewhat infiltrated; its mucous membrane was bleeding, and during the introduction of the instrument a slight resistance was felt at this point. A week later, as the chief of the gastro-enterologic department wanted to see the picture, gastroscopy was repeated. In this short time the changes had increased considerably, and the cardia was definitely involved; an ulceration was also seen. Dr. Palmer decided against a laparotomy after being shown these findings. In this case, again, gastroscopy showed much more detail than the roentgenogram. (See *B* in the color plate.)

Operable Tumors.—In this discussion we shall briefly refer to cases 5, 6 and 7 and present three others. In case 5 operability was shown after gastroscopic examination by the fact that the tumor was seen only on the angulus. Operability was deemed likely in case 6, but we could not be certain since the gastroscopic picture showed the edge of the ulcer passing into the normal mucous membrane. However, it could not be said that operation was out of the question. Practically the entire stomach and a large section of the transverse mesocolon were resected. Certainly the gastroscopic picture gave a more correct impression of the seriousness of the case than did the roentgen examination. In case 7, we stated, after gastroscopy, a half-year before the operation, that the tumor would be operable. If the patient had been convinced of the necessity of the operation earlier he might have survived, since the lesion was relatively benign and well confined. This case illustrates the obvious fact that an early diagnosis is of little value if the patient will not cooperate.

CASE 11.—History.—A man aged 63, seen on Aug. 1, 1934, for the past twenty-five years had epigastric distress consisting of a localized burning pain occurring two or three hours after meal time and at about 2 a. m. This distress was always relieved by the ingestion of food. On two occasions his condition was diagnosed as a gastric ulcer. Since June 1933 his distress had changed somewhat. He complained of dull epigastric pain associated with fulness immediately after eating. His appetite had been poor, and he had lost 15 pounds (6.8 Kg.) in weight.

Physical Examination.—A questionable mass was felt in the epigastrium; otherwise the results of the examination were negative.

Laboratory Examination.—The gastric fluid obtained after an Ewald test meal showed: free acid, 29, and total acid, 75. The stools gave a 4 plus reaction to the benzidine test for blood.

Roentgen Examination.—The picture was that of carcinoma of the stomach with partial obstruction. The upper two thirds of the lesser curvature appeared pliable and did not appear to be infiltrated. The lower three fourths of the greater curvature also appeared to be pliable, with no infiltration. The patient would not give permission for operation. He was readmitted to the hospital on December 21.

Clinical Impression.—On the basis of the clinical picture the condition was thought to be a large carcinoma of the stomach, probably inoperable, but with no demonstrable metastases.

Gastroscoy (December 24).—The pylorus was instantly seen. It was a small, completely rigid hole, the posterior wall of which was covered by a prominent round tumor on which were seen two nodes. The border was well marked except for the posterior side, where no real edge could be seen. At this point there seemed to be a diffuse infiltration of the posterior wall where the mucous membrane was very thin, and a large blood vessel could be observed. The upper portions of the posterior wall, however, were quite normal, as were all the other portions of the mucous membrane except for being somewhat more pale than usual. The distal node of the tumor showed a pink and spotted mucous mem-

